THE ANNALS

OF OTOLOGY RHINOLOGY & LARYNGOLOGY

NNALS PUBLISHING COMPANY — SAINT LOUIS 88, MISSOURI

OLUME LXX SEPTEMBER, 1961 NUMBER 3

THE ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY
Published Quarterly by
THE ANNALS PUBLISHING COMPANY, St. Louis 5, Mo., U. S. A.
Entered at the Postoffice, St. Louis, Mo., as Second-class Matter

All Manuscripts and Other Editorial Matter Should Be Addressed to the Editor
12 WESTMORELAND PLACE, ST. LOUIS 8, MO.

Subscriptions,
Purchase Vouchers,
and All Business Communications Should Be Directed to the
ANNALS PUBLISHING COMPANY
P. O. BOX 106, CLAYTON STATION 5, ST. LOUIS, MO.

In notifying the business office of change of address,
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INFORMATION

FOR CONTRIBUTORS

INSIDE BACK COVER

ANNUAL SUBSCRIPTION

In Advance

United States, $16.00 Canada, $16.50 Other Countries, $17.00
Special Rate for Students, Internes and Residents, $10.00 per Annum

ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY

FOUNDED IN 1892

VOLUME 70

PUBLISHED QUARTERLY

BY THE

ANNALS PUBLISHING COMPANY

EDITORIAL OFFICE • 12 WESTMORELAND PLACE, 8

BUSINESS OFFICE • P. O. BOX 106, CLAYTON STATION, 5

SAINT LOUIS, MISSOURI, U. S. A.

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SIGNIFICANCE AND MANAGEMENT OF ORBITAL, FACIAL AND NECK SWELLINGS

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The most experienced clinician is frequently challenged when confronted with a patient presenting himself with a swelling in the head and neck areas. While from a practical point of view, an absolute diagnostic formula may not be possible, a certain pattern is shared by the various anatomical sites that lend themselves to classifications featuring congenital, constitutional, inflammatory (acute and chronic), traumatic, and neoplastic (benign and malignant) divisions, modified somewhat by the morphologic terrain. There are other features that the various areas have in common such as, the unsightliness of the swelling and the interference with essential functions. The interference with vital functions, the result of bone involvement by direct extension (continuity and contiguity of structure) via foramina, dehiscences, perineural sheaths, vascular and lymphatic channels, and along fascial planes, poses a threat to the eye, to the brain and to the airway. Neoplasms, even though histologically benign, may be viewed as clinically malignant because of their progressive, expanding growth tendencies.

Identification of a swelling in the frontal region, orbit, maxilla, or neck often presents a perplexing problem. All things may happen

Presented as one of the Sommer Memorial Lectures, Portland, Oregon, April, 1961.

to all men and the areas under discussion are no exception. Even the most experienced observer can ill afford to relax his vigilant approach to correct diagnosis. Repetitious as it seems, and as much as it would appear that only the medical student should be required to indulge in that favorite exercise of differential diagnosis, it behooves the clinician to assume the attitude that the diagnosis of a swelling can in itself be a challenging research problem. An occasional "snapshot" or intuitive diagnosis which proves in error, will soon dispel any notions of diagnostic infallibility, or clinical invincibility. It is for this reason that it is appropriate that the clinician constantly have before him the recognized patterns of differential diagnosis. The rare case, while so frequently housed in the museum or recorded in the literature for posterity, may appear in person on any given day in a physician's office. Routine minimizes the chances for oversight or error.

CLASSIFICATION OF ORBITAL AND FACIAL SWELLINGS

Swellings associated with the orbit and face, including the nose, nasal accessory sinuses and maxilla present themselves in a variegated array of differential diagnosis:

I. *Congenital*

1. Dermoid
2. Cephalocele and meningocele
3. Angioma
4. Craniofacial synostosis
5. Teratoma

II. *Inflammatory*

1. Acute
   a. Sinus disease
   b. Periostitis
   c. Cellulitis
   d. Osteomyelitis
   e. Cavernous sinus thrombosis
   f. Erysipelas and various dermatoses
   g. Parotitis

h. Dacryoadenitis

i. Mastoiditis (zygomatic)

2. Chronic

a. Sinus disease

b. Osteomyelitis

c. Nephritis

d. Trichinosis

e. Syphilis (gumma)

f. Tuberculosis

g. Echinococcus

h. Allergic

i. Hematopoietic disturbances

j. Graves' disease (early)

III. *Trauma*

1. Hematoma

2. Fracture

3. Emphysema

4. Foreign bodies

IV. *Neoplastic*

1. *Intracranial,* located in the anterior fossa above the orbital roof: chiasmal area, pituitary region, middle fossa.

2. *Orbital cavity:* hemangioma, meningioma, dermoid, melanoma, hypernephroma, neuroblastoma, sarcoma, mixed tumors of lacrimal gland and inflammatory pseudotumors.

3. *Nasal cavity:* angiofibroma, polyps, inverting papilloma, chondroma, neurofibroma, hemangiomas, mixed tumors, various types of carcinoma, and malignant connective tissue tumors.

4. *Paranasal sinuses:* mucocele and cysts (secreting and nonsecreting), osteoma, Paget's disease, malignant tumors.

5. *Nasopharyngeal space:* angiofibroma, chordoma, craniopharyngioma (Rathke pouch tumor), epidermoid carcinoma and reticulum cell sarcoma.

SWELLINGS ABOUT THE ORBIT

There are general criteria which the clinician finds useful in differentiating causes of unilateral or bilateral proptosis of the eye. In regard to the latter, bilateral exophthalmos is observed in constitutional diseases such as Graves' blood disturbances and xanthomatosis, with the exception that exophthalmic goiter may occasionally be unilateral. Inflammatory and noninflammatory disease usually leads to unilateral proptosis, an exception being an occasional instance of cavernous sinus thrombosis producing a bilateral involvement. Inflammatory exophthalmos is usually accompanied by signs and symptoms such as fever, leukocytosis, increasing proptosis and with it comes an interference with motility of eyeball.

The direction of the proptosis is an important diagnostic clue. If the eyeball is displaced downward and nasally, a dacryoadenitis (if inflammatory), or a lacrimal gland tumor in the upper outer quadrant of the orbit, may be suspected. If, however, the eye is pushed up and out, or up and in, a likely possibility is a malignant tumor of the maxillary sinus. Lateral protrusion of the globe suggests tumors of the ethmoids and sphenoids. Such bilateral involvement produces the typical "frog face" appearance. A downward and outward displacement of the eyeball suggests a subperiosteal abscess or a mucocele of the frontal and ethmoid sinuses. When accompanied by inflammation the latter may be a pyomucocele. Cephaloceles and meningoceles are manifested as firm fluctuating masses at the upper inner angle of the orbit. If the contents of the orbit are pushed straight forward, especially when accompanied by limitation of motion, a mass in the muscle cone is suggested.

The most frequent cause of swellings about the eye is inflammatory disease of the sinuses which in turn may affect the components of bone and the adjacent tissues or cavities. The next most frequent cause is a mucocele or cyst which can expand in any direction and produce an alteration in orbital or facial contour. In the next order of frequency would then be the group of neoplasms within the nasal cavities and orbit. The recognition and management of the more commonly encountered conditions are selected for the ensuing discussion.

Congenital cysts of the head are classed in accordance with their germ cell layer origin as ectodermal, entodermal and mesodermal. Epidermoids are derived from displaced ectodermal elements which develop into epithelial lined pouches. They are located deep in the corium, most frequently in the embryonic lines of closure, at the root of the nose, the lower lip and the floor of the mouth. The content of such cysts is made up of lamellated keratin, serous or caseous material. The wall is composed of fibrous tissue lined by stratified and cornified epithelium. This is different from dermoids, which are commonly found deeply situated over the nasal dorsum and occasionally in the internal or external canthi, in the eyelids and conjunctiva, in the orbit and in the nasolabial fold. The wall of a dermoid is lined by epidermis which includes rudimentary sebaceous and sweat glands, hairs and sebaceous material.

Dermoid cysts of the nose are usually present at birth, but they may not become evident until much later. In many instances they are not diagnosed and therefore incorrectly or inadequately treated until someone recognizes the embryologic background and its morphologic variations. So very often they erroneously are diagnosed as "just a pimple." Trauma may activate the process of development and growth. Other congenital anomalies are seldom associated, and heredity plays a minimal role.

The cyst usually presents as a localized swelling in the midline anywhere from the glabella to the tip of the nose, with its greatest incidence on the upper part of the dorsum. The swelling is usually globular, fluctuant to palpation and not adherent to the skin. The lesion may also present as a pimple or a dimple on a slightly broadened nose. Trauma, infection and manipulation are generally followed by multiple fistulas. When a fistula is present, sebaceous material and sometimes a few hairs may emerge from the opening. An infection or the intermittent discharge is most frequently the major concern of the patient. The sinus tract usually involves the frontal or the nasal bones and the cartilages of the nose. Injection of radiopaque substances into the skin opening may reveal the course of the sinus tract and the cyst.

The differential diagnosis includes epidermal and sebaceous cysts, meningocele, lipoma and other connective tissue tumors as well as specific granulomatous diseases. The only adequate treatment of dermoid cysts of the nose is total surgical excision. Longitudinal or transverse incisions are to be used, according to the site and extent of the lesion, in order to achieve optimal esthetic results. The removal

of uncomplicated cysts and sinuses is usualy simple and effective. Instances in which there has been previous infection or manipulation may present difficulties in identification of the sinus tracts and stalk because of scar tissue. Sacrifice of bony or cartilaginous structures may be necessary in such cases.

Cephalocele, a herniation or meninges, brain substance or both, may present itself extranasally between the frontal and nasal bones or through a dehiscence in the mesial wall of the orbit. Patients present themselves with a widening of the bridge of the nose, increasing the canthal width as well. The eye deformity is brought about by a displacement downward, outward and forward, which may or may not be accompanied by visual disturbances (limitation of motion, ptosis, and possibly, diplopia). Patients complain of headache, nasal blockage and at times, cerebrospinal rhinorrhea.

Mucoceles are secreting cysts formed by the accumulation of the products of secretion, desquamation and inflammation within the frontal sinus, with subsequent distention of its walls. Further expansion is facilitated by obstruction of the nasofrontal duct. Repeated regional infections, trauma and neoplasm, especially nasal polyps, play a role in permanent blockage of the duct. There is frequently a history of previous frontal sinusitis, occasionally accompanied by external swelling. As secretion gradually accumulates, there is a feeling of distention and neuralgic-like pain and sensitivity to palpation. As the mucocele increases in size, it may expand to thin out or erode the bony wall of the orbit, nasal cavity, anterior cranial fossa, the floor or the anterior wall of the frontal sinus. External deformity varies in site and size. The down and outward displacement of the eyeball is so slow in developing that diplopia, visual impairment, limitation of movement of the globe and ptosis of the lid may not be noticed by the patient. Cysts, containing a greenish or brownish viscid fluid, when infected, may lead to a pyocele. Mucoceles and cysts require an external frontal sinusotomy exposure through the eyebrow for complete removal of the lining membrane and floor of the frontal sinus and all of the fronto-ethmoid cells which are usually affected. A large opening is provided into the nose to prevent closure of the duct and recurrence of the mucocele.

Osteoma is a frequently encountered space-filling lesion of the frontal sinus which has the same propensity for thinning and erosion of its walls in any direction as does the mucocele. When small, it is a chance finding in x-rays taken of the head. External deformity is the presenting symptom with displacement of structures such as the

eyeball, the nose or the forehead. Osteomas are sessile or pedunculated, frequently situated at the suture line between the frontal and ethmoid bones. When the direction of growth is toward the brain, headache, epileptiform seizures, cerebrospinal rhinorrhea and pneumoencephalus are possibilities. Meningitis and brain abscess are occasional complications. The surgical approach to the osteoma is by the external route, the incision being made through one or both eyebrows, depending upon the size and extent of the mass. The brow incisions may be joined over the nasal glabella and the drainage provided through the interior of the nose.

Many clinicians believe the new bone formation of osteomas to be due to trauma but others think of them either as embryologic or infectious in origin. There is, however, a condition which involves cranial and sinal areas, generally designated as a fibrous dysplasia of bone or ossifying fibroma, in which a perverted activity of bone-forming mesenchyme leads to facial deformity. The nasal accessory sinuses become filled with newly formed tissue. The alteration in contour is not accompanied by pain but the nasal cavity can become obstructed, eye changes may ensue due to displacement and even the eustachian tube orifice may be impinged upon. Such extensive involvement does not lend itself to surgical resection. Clinically, the differential diagnosis between carcinoma, sarcoma, osteoma, osteochondroma, ameloblastoma, eosinophilic granuloma, osteitis fibrosa cystica, osteomyelitis, and the like, makes for interesting analysis.

The proximity of the anterior ethmoid cells to the frontal and maxillary sinuses readily exposes them to extension of infection. Purulent inflammation of the nose causes a tissue reaction which interferes with normal ventilation and drainage of the sinuses. One form of acute ethmoidal sinus disease occurs especially in infants and young children, manifesting itself rather violently by external swelling about the face, osseous involvement, and frequently complicated by intracranial extension. Caries and inflammatory erosion of bone (osteoclasis) result from extreme pressure by inflammatory products, effecting a separation of the bone from its mucous membrane and mucoperiosteum. It is estimated that three-fifths of orbital complications originate from the sinuses. Conversely, two to three per cent of sinus infections are complicated by orbital infections. Another small percentage of involvements occur following intranasal surgical procedures on the ethmoid labyrinth. If the nasofrontal duct is obstructed, the frontal sinus becomes distended. Intrasinus pressure may become so great as to interfere with circulation of the underlying bone, encouraging the invasion of the soft tissues (periosteum, marrow

and endosteum). A suppurative process may extend through the sinus wall and pass into the orbit, the nasal, or cranial cavity. Clinically, osteomyelitis may be acute, chronic or latent, be self-limited and protracted or diffuse and progressive, spreading to all parts of the skull.

Naso-orbital extension of osteomyelitis frequently is associated with redness and swelling around the eye and forehead. The degree of these manifestations would depend upon the pathologic pattern and the clinical stage of the disease. At times the stimulation of osteoplastic function can obliterate the sinus. What the clinician needs to know is that while this new bone formation constitutes a healing process, the osteoplastic process is still possible when incited by trauma, swimming and acute exacerbation of neighboring sinus disease. The "all or none law" seems to prevail in the surgical attack on osteomyelitis of the skull which, by the way, is not the prototype of long bone osteomyelitis. The morphogenesis and the proximity to vital structures of and in the brain make it different. Either the involved bone is to be resected widely or not interfered with at all because simple drainage or piecemeal surgery can prove to be disastrous. Antimicrobial therapy is employed but in itself cannot combat osteomyelitis of the skull.

A discussion of acute infections about the face which may lead to swellings about the orbit cannot be concluded without mention of cavernous sinus thrombosis. Venous radicals can carry infection from a number of sources:

1. *Anterior foci* (lip, ala nasi, vestibule of nose and eyelids), spreading by way of the frontal, anterior facial, angular, supraorbital and supra-trochlear veins to the ophthalmic veins.

2. *Internal foci* (sinuses, turbinates and septum), carried by the ethmoidal veins or through the wall of the sphenoid sinus.

3. *Inferior foci* (pharynx, superior maxilla and deep cervical area), extending by way of the pterygoid plexus or by direct proximal extension of the internal jugular through the lateral sinus and the petrosal veins.

4. *Posterior foci* (middle ear and mastoid), by extension from the lateral sinus through the petrosals, especially inferior, and the carotid plexus of veins in close proximity to the tympanic cavity.

5. *Contiguous foci* (sphenoid sinus, posterior ethmoid sinuses and petrous apex of the temporal bone).

The symptoms and signs of cavernous sinus thrombosis represent a severe acute infection, characterized by local and constitutional phenomena of a terrifying nature. There is chemosis of the bulbar conjunctiva, edema of the eyelids and exophthalmos. Swelling or firm induration and tenderness is present over the face or forehead when the nasal accessory sinuses are affected. Involvement of the 2nd, 3rd, 4th, ophthalmic division of the V, and the VI nerves may become evident. Chills, fever, nausea and meningeal symptoms may be present. The full complement of antimicrobial drugs, heparin and dicoumarol have supplied a more hopeful outlook for cavernous sinus thrombosis. The best treatment to date is still prevention.

Neoplasms which arise from the nasal cavity represent those tissues which constitute it, and secondarily involve the neighboring structures or spaces. They may be small benign growths or invasive malignant tumors or they may be extensive benign growths or invasive malignant tumors which produce varying degrees of swelling and present problems both in diagnosis and management. Tumors of the nasal cavity frequently present unusual problems of diagnosis and treatment. Signs and symptoms consist of nasal obstruction, discharge, bleeding and facial swelling or deformity. Early, the obstruction may be of a mild degree, but it is unilateral and persistent. Bleeding, likewise, is usually unilateral, and may be so scant that it only streaks the mucus, or massive. The fact of the matter is that bleeding may be more severe in certain forms of benign neoplasms than in malignant ones. This is especially true of angiofibromas.

Polypoid changes in the nasal mucosa are frequent in the presence of others forms of neoplasms. Large polypoid masses may accompany the histologic change of the tumor, or it may be associated with the increasing pressure within the nasal cavity. The development of large nasal polyps may mask the underlying neoplastic changes both grossly and on repeated histologic study. Care must be taken to evaluate the condition correctly so that it not be considered just nasal polyps, thereby losing valuable time for successful intervention. Adequate tissue for biopsy is essential.

All tissue removed from the nose must be examined microscopically, even though it may appear grossly to be a benign polyp. Rapid recurrence of polypoid tissue, after thorough removal is a warning that the underlying process is malignant. Where there is doubt or

where previous biopsy or biopsies have revealed only polypoid change, a more adequate biopsy under hospital or surgical conditions may be advisable in order to obtain sufficient tissue and to be in a better position to manage possible severe hemorrhage. Office biopsy frequently proves inadequate because removal of superficial bits of tissue result from the concern for bleeding, or technical difficulties encountered in trying to snare tissue from a large or firm mass. Repeated biopsies, stained smears, or aspiration biopsy may be necessary whenever suspicion of the histological character of the tumor is not confirmed by the original biopsy, especially when an obstructive mass persists. Whenever tissues are removed bilaterally, specimen material from each side should be bottled separately and labeled accordingly.

Benign tumors arising in the nasal cavity originate from the representative tissues of that area. There are certain tumors which by their very location near vital areas and by their progressive, expanding growth tendencies may be considered histologically benign but clinically malignant. Such growths may evidence a benign histologic pattern with some orderliness of growth, but the clinical course may be a progressively destructive one with subsequent involvement of the surrounding nasal bones, nasal accessory sinuses, orbit, cribriform plate, and cranial cavity. Malignant tumors demonstrate the characteristic features of malignancy such as anaplasia, infiltration, and destruction, rapid and uncontrolled growth, variability in size, shape and staining properties of the cells, and metastases.

Diagnosis of a tumor of the nasal cavity requires a careful evaluation of the history, thorough anterior and posterior rhinoscopy, multiple, correctly positioned x-ray studies, and an adequate biopsy. The value of an x-ray assessment may be enhanced by laminagraphic studies which may reveal the site of origin of the neoplasm. Benign tumors which produce obstruction may evidence an opacity of the nasal fossa associated with clouding of the accessory sinuses. There may be some thinning of bone and destruction by pressure necrosis when structural displacement occurs. Similar opacification may be produced by malignant tumors, but in addition, there may be an obvious break in the continuity of the bone, frequently associated with markedly irregular destruction. Clouding in the sinus areas is not always to be regarded as evidence of extension of the tumor, since an obstruction of the sinus ostium may produce an increased roentgenographic density due to lack of aeration or to secondary infection.

Treatment of tumors of the nasal cavity varies with the histological character and extent of the lesion. Therapy is essentially surgical,

consisting of wide excision of the involved tissues as the chief means of attack. Extensive benign and malignant tumors require more adequate exposure of the nasal cavity for an assured complete removal. Inasmuch as the surgical approach is made through and into a very vascular bed, careful preoperative medical and surgical preparation and planning is essential.

The chief objectives of major tumor surgery of the nasal cavity are adequate exposure, satisfactory hemostasis, and thorough excision of the tumor. Exposure of the nasal cavity is best obtained either by lateral rhinotomy alone or combined with the Fergusson incision through the upper lip. The extent of the surgical resection after the exposure has been effected is dependent upon the findings within the nasal cavity. Benign tumors may be so extensive as to require resection of the entire lateral nasal wall, including the turbinates together with a portion of the nasal bones and ascending process of the maxilla. Malignant tumors may invade the ethmoid cells, maxillary sinus, palate and orbit. The possibility of palatal resection with or without orbital exenteration enters into the pre-operative planning. Occasionally, it is necessary to sacrifice the overlying skin and later consider a suitable prosthesis or plastic repair.

SWELLINGS OF THE NECK

Swellings of the neck have been described since antiquity when simple goiter was recognized 1500 years B.C. by the Chinese and later described by the Greeks and Romans. Yet today, tumors of the neck continue to present many interesting and, at times, puzzling and difficult, problems of diagnosis and management. These swellings may vary in severity from a simple epidermal cyst to a carotid artery aneurysm. They may in themselves be the entire disease process or they may only be the presenting finding of other serious underlying disease. Characteristically, a patient recently was observed who presented with a progressive painless swelling in the upper neck. He had been admonished by his physician, "As long as it does not bother you, do not bother it." Bothering it by aspiration biopsy revealed metastatic cancer and permitted correct treatment much later than it should have been applied.

Accurate diagnosis is essential to proper management in this condition as in all of medicine. A detailed history may provide the most significant information. Pain, fever and sore throat may suggest an infectious origin. Injury, bleeding, hoarseness or cough may indicate other possibilities. A thorough examination of the head and

neck adds to this information. This must include not only the nose, throat and ears but the entire oral cavity, palate, floor of mouth, nasopharynx, larynx, hypopharynx, sinuses, and neck. In the neck, certain characteristics of the mass may provide valuable leads. Its location is often a guide. Midline swellings may be cysts of congenital origin while lateral swellings have neoplastic implications.

The size and shape, definition of margins, consistency, tenderness (whether expansile or transmitted), direction of movement on swallowing, warmth, pulsation, compressibility, and mobility may aid in the differentiation of the swellings. Palpation and auscultation may prove of valuable assistance in addition to inspection. Bimanual palpation, with one finger in the mouth, is helpful. Venous humming sounds warn of an aneurysm or the gurgle or thud on swallowing when listening to the neck by means of a stethoscope are important diagnostic clues.

Laboratory tests may provide additional clues. X-ray studies of the chest, sinuses and neck region may prove helpful. Additional diagnostic procedures may include bronchoscopy, esophagoscopy, skin tests, gastro-intestinal series, and iodine uptake studies. Finally, biopsy or excision may be necessary to establish the diagnosis. Biopsy of a primary tumor or apiration biopsy of a neck mass may be done.

In summary, the diagnosis of a mass in the neck and subsequent proper management are based on: 1) careful history, 2) thorough physical examination of the head and neck, 3) laboratory tests, 4) x-ray studies, 5) special examinations and 6) biopsy.

Swellings of the neck may be classified into several large categories including congenital, inflammatory, traumatic and neoplastic.

CLASSIFICATION OF NECK SWELLINGS

A. *Congenital*

1. Epidermal cyst
2. Dermoid cyst
3. Branchial cleft cyst
4. Thyroglossal duct cyst
5. Cystic hygroma colli
6. Congenital muscular torticollis
7. Laryngocele
8. Aneurysm
9. Ranula

B. *Inflammatory and traumatic*

1. Hematoma
2. Non-specific cervical adenitis
3. Tuberculous adenitis
4. Boeck's sarcoid
5. Cellulitis of the neck
6. Deep cervical abscess
   a. Submandibular space infection
   b. Parpharyngeal space infection
   c. Ludwig's angina—submental swelling
   d. Bezold mastoid abscess—digastric space
7. Infectious mononucleosis
8. Subacute thyroiditis
9. Syphilis (adenitis and gumma)
10. Parotitis

C. *Neoplastic*

1. Benign
   a. Thyroid tumors
   b. Lipoma
   c. Fibroma
   d. Chondroma
   e. Neurofibroma
   f. Dermoid
   g. Keloid
   h. Hemangioma
   i. Lymphangioma
   j. Benign salivary gland tumor
   k. Carotid body tumor
2. Malignant
   a. Lymphoma
   b. Leukemias
   c. Branchiogenic carcinoma
   d. Thyroid carcinoma
   e. Malignant salivary gland tumors
   f. Metastatic carcinoma

Congenital lesions in the neck which produce enlargements of the neck include a variety of cysts and masses. Some are superficial and develop in the skin. These include the epidermal cysts which may occur anywhere in the skin of the neck, are readily diagnosed, and are treated by complete excision. Dermoid cysts are usually single enlargements and usually occur in the midline of the neck.

Thyroglossal duct cysts also develop in the midline. Their origin is from the tract of the developing thyroid gland which originates at the base of the tongue (*foramen caecum*) and ends in the region of the thyroid isthmus. Such cysts may occur anywhere along this path and manifest themselves at any age. They usually pass through the hyoid bone so that complete surgical removal must include a central portion of the hyoid bone as the tract is dissected to the base of the tongue.

Not all congenital cysts develop in the midline. Those of branchial cleft origin appear in the upper lateral neck, usually beneath the sternomastoid muscle. Their tract often passes between the external and internal carotid arteries to open into the lateral wall of the pharynx near the upper pole of the tonsil or to end blindly at that location. Branchial cleft cysts are smooth, firm, fluctuant masses which may become secondarily infected. On aspiration of their contents, cholesterol crystals are found and establish the diagnosis with certainty. Treatment consists of thorough surgical excision.

Cystic hygroma colli and congenital muscular torticollis are not congenital lesions in a true sense of the word. The cystic hygroma is in reality a lymphangiomatous tumor made up of large lymph-filled spaces lined by a delicate endothelium. These tumors frequently develop in young infants or children and may extend rapidly to infiltrate the structures of the neck. They are often large, soft, nontender somewhat fluctuant masses occurring in the submaxillary or supraclavicular areas and extending to adjacent regions of the neck. Surgical excision is the treatment of choice. In many instances they extend so widely that only partial removal is safe or even possible. Congenital muscular torticollis is a tumor mass affecting the sternomastoid muscle, made up chiefly of a mass of fibrous tissue and thought to result from ischemic necrosis in that muscle. It resembles a tumor and removal of the fibrosed band releases the shortened muscle and relieves the abnormal twisting of the neck.

Laryngocele is an unusual, soft and intermittent swelling of the neck which is both of congenital origin and, at times, made apparent or aggravated by persistent trauma. It is produced by increased intralaryngeal pressure, as in certain occupations (glass blowers and wind instrument musicians) in which a small outpouching of the ventricle of the larynx is progressively enlarged. This saccule soon extends to the thyrohyoid membrane and then bulges through it into the soft tissues of the neck making its appearance just to the right or left of the midline at the greater horn of the hyoid bone. On pres-

sure, it may collapse completely, only to fill with air again when the patient strains. X-rays of the neck reveal a typical air shadow which absolutely is characteristic of this pathologic change. When the laryngocele is an internal one, also involving the false vocal cord, there may be marked respiratory obstruction and severe hoarseness. Treatment of this condition, as with most congenital cysts and masses, consists of thorough external surgical removal.

Swellings of inflammatory and traumatic origin may develop in any location in the neck. Hematoma occurs after direct trauma, most commonly from a tear of the muscle and often into the sternomastoid muscle. Nonspecific cervical adenitis may develop in any of the many lymph nodes of the neck, but most frequently in the deep jugular chain near the angle of the mandible. Dental infection, tonsillitis, and pharyngitis are the most common underlying causes. These nodes are firm, smooth and quite tender. They may enlarge to huge proportions and suppurate to produce an abscess. Much reduced in incidence following the introduction of antibiotics, they are being seen more commonly with the development of more resistant strains of organisms.

Other inflammatory swellings that are encountered are tuberculous adenitis, Boeck's sarcoid, and cellulitis of the neck. Deep cervical abscess develops in the potential spaces of the neck secondary to dental or pharyngeal infection. This may occur in the parapharyngeal space, the submandibular space, or in the floor of the mouth and submental region as Ludwig's angina. Treatment consists of the employment of appropriate antibiotics in adequate dosage, heat, and correct incision and drainage. In many of these patients, encroachment on the airway demands a tracheotomy before any anesthesia is given for surgical drainage. Disaster may follow anesthetic efforts if the airway is inadequate.

The location of tumors of the neck is frequently suggestive of the diagnosis and, in certain cases, is pathognomonic. Anteriorly, in the midline to be considered are thyroglossal cyst or fistula, dermoid cyst, thyroid isthmus tumor or enlargement, thyroiditis, or lymphadenopathy. In the submaxillary and parotid areas, submaxillary gland tumors, parotid tumors, submaxillary sialadenitis due to a calculus, mumps, nonspecific parotitis, lymphadenopathy, or submandibular space infection may be considered. Lymph node involvement may be specific or nonspecific and, in some instances, represent metastatic tumor.

Lateral neck tumors include branchial cyst, neurofibroma, metastatic carcinoma, lymphadenopathy, cystic hygroma, carotid body tumor, and lymphosarcoma. Thyroid lobe enlargement is usually so characteristic at the location of the thyroid gland that it provides little diagnostic difficulty. Lateral aberrant thyroid, which is really metastatic carcinoma of the thyroid, may produce a tumor in the upper lateral neck. Many other tumors may occur in this region but are less commonly encountered. These include laryngocele, esophageal diverticulum, and carotid artery aneurysm.

Treatment of tumors of the neck is dependent on the diagnosis. Cysts, epidermal, thyroglossal, branchial and dermoid, are best treated by complete surgical excision. Benign tumors, which often produce discrete, firm, movable nontender masses, can often be completely removed surgically and may demand no other treatment.

Inflammatory lesions, however, may require a combined therapeutic regimen. Antibiotics are specifically employed as indicated by sensitization studies. Chemotherapeutic agents may also be required. Surgical drainage may be necessary despite all medical efforts. Tuberculous adenitis may demand long term treatment with streptomycin, INH and PAS. Infectious mononucleosis and specific mycotic infections demand special diagnostic procedures.

Metastatic carcinoma may provide many difficult problems of diagnosis and treatment. It is one of the commonest causes of a swelling of the neck and may be the first symptom of serious underlying disease. In cancer of the nasopharynx, for example, the enlarged node in the upper neck may be the only symptom which brings the patient to the physician. Such nodes are hard, often fixed, usually lateral near the angle of the mandible, or at the bifurcation of the carotid, and may be single, multiple, or constitute one large firm mass. Aspiration biopsy will reveal metastatic carcinoma. Careful search for a primary in the head and neck and their various recesses, is imperative. Treatment must combine management of the primary tumor with that of the metastatic nodes. Treatment varies in accordance with the location of the primary. Treatment of the cervical metastases is usually surgical, demanding radical neck dissection when the primary tumor can be controlled. In many instances (tongue, alveolus and larynx), surgical treatment of the primary and neck metastases is the treatment of choice, with combined removal in continuity.

Parotid gland swellings may appear either in the facial region, the upper neck, or both, because of the anatomical location of the

gland. These swellings may be the result of functional disorders, acute infections, obstructive states, specific types of inflammation, cysts, benign or malignant tumors.

One of the commonest causes of parotid swelling is epidemic parotitis or mumps. The disease is caused by a virus and may be unilateral or bilateral. The condition requires no specific therapy but the use of immune globulin after known exposure may aid in modifying the course of the illness. Suppurative parotitis frequently is a serious complication of major surgical procedures in debilitated individuals. In such instances there is rapid development of an extremely painful swelling with attendant fever, leukocytosis, general weakness and malaise. A large abscess may develop within the substance of the gland, necessitating incision and drainage if the infection is not controlled by the use of heat and a definite antibiotic therapy. Cultures often reveal resistant staphylococci. Other conditions which may result in inflammatory swelling of the gland include salivary duct calculi and Mickulicz disease, with diffuse inflammation of the entire structure.

Cystic swelling of the parotid may occur with certain benign tumors or result from the development of a true cyst, either a retention cyst or a branchial cyst. Retention cysts are lined by a flattened or cuboidal epithelium and are the result of obstruction of one of the ducts with a resultant dilatation of the duct behind the point of obstruction.

Branchial cysts of the parotid are rare. Much more commonly do they occur in the upper neck beneath the sternomastoid muscle. Occasionally they may develop within the substance of the parotid gland with a characteristic stratified squamous epithelium and an infiltration of lymphocytes beneath the epithelial lining. Treatment of cysts of the parotid consist of thorough surgical excision. The prognosis is excellent.

Parotid tumors may be benign or malignant. The commonest tumor in this region is the mixed tumor, considered by most authorities to be benign, but occasionally showing characteristics of true malignancy. A tendency to recur following limited excision is a common experience. The exact histologic nature of this tumor has been debeated by pathologists for over a century, but the consensus today is that it is an epithelial tumor surrounded by other tissues. As a rule it is slow growing. It is frequently present for many years before the patient consults the physician. Though the parotid gland

is in intimate association with the facial nerve, most benign tumors do not produce either facial weakness or paralysis. The presence of facial paralysis and a parotid tumor, however, is suggestive of malignancy in the tumor with actual invasion of the nerve.

The treatment of mixed tumor is essentially surgical. Since many reported series have indicated a high incidence of recurrence with local excision, it has been the accepted practice to excise the entire lateral lobe of the parotid containing the partially encapsulated mixed tumor. Tumors involving the deep lobe demand total parotid excision. Every effort is made to expose the facial nerve carefully and to preserve it by meticulous dissection in the presence of a benign tumor. Other benign tumors which may occur in this region are adenoma, lipoma and fibroma. Treatment of these is also surgical.

An interesting and unusual benign growth often develops in the "tail" of the parotid in the upper neck. This is the papillary cystadenoma lymphomatosum or Warthin's tumor, a soft, cystic, movable, nontender mass usually occurring in older persons, and most often in males. It is a benign tumor made up of typical epithelial elements combined with masses of normal lymphoid tissue in a classic pattern. Diagnosis clinically is not difficult, and treatment consists of surgical excision of the tumor.

Malignant tumors of the parotid present much more difficult problems of therapy. These are often rapidly growing, fixed, hard, painful or tender masses which may invade the facial nerve and produce partial or complete facial paralysis. There may be local metastasis producing enlarged, firm regional nodes. In such cases, the surgeon must be prepared to do a wide local excision combined with neck dissection. The patient must be prepared for the possible deliberate sacrifice of the facial nerve under these circumstances as it is necessary to excise the entire tumor. Malignant tumors of the parotid may vary in aggressiveness from that of the low grade mucoepidermoid carcinoma to the relentless, recurring, steadily progressing adenocarcinoma or epidermoid carcinoma.

1853 W. Polk Ave.

XLIX

TRANSITORY PHENOMENA IN AUDIOMETRIC DIAGNOSIS

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According to Pimonow,[13] a transitory phenomenon may be identified with a disturbance or a temporary, powerful equalization, which exhibits a mixture of vibrations, the frequencies, phases and amplitudes of which vary in time.

The auditory centers receive their information through a system of analysis, and comprehension is bound up with the integration of elements of information. If it is admitted that a periodic vibration is a phenomenon which is exactly established in the past and the future, that it cannot transmit unknown elements, it is obvious that audiometric tests for the purpose of examining the functioning of the auditory passage may be carried out by utilizing variations of the permanent system, as well as by its appearance or disappearance, which implies a succession of transitory phenomena.

The measurement of hearing makes it possible to study the function of a receiver and to estimate the possibilities of a sound signal which is considered as an element of information and which must provoke the expression of a response. Although it is not necessary for the auditory cortex to be intact in order to obtain a response to a sound stimulus, it has however always seemed possible that certain cortical or mesencephalic lesions may determine the pathological characteristics of hearing; the appearance of these characteristics presupposes a possibility of examining the whole functioning of the auditory passage.

Although the various writers on the subject may not have stressed or even remarked on it, tests utilizing a determination of auditory fatigue, measurement of the time of response, or an identification of interrupted words, all constitute a study of transitory phenomena; consequently there already exists a clinical audiometry, an important series of tests utilizing transitory phenomena for purposes of diagnosis.

FIRST EXPERIMENTS

The effect of fatigue has been studied for many years and numerous writers have contributed a great deal of information to the understanding of the responses of the auditory apparatus after stimulation.

Hood,[10] in particular, has drawn attention to the advantages of utilizing a modulated signal.

Causse and Chavasse[5] have demonstrated the advantages of utilizing frequencies above 500 cycles.

Munson and Gardner have utilized the same frequency for stimulation and for the test sound.

At the present stage, audiometric methods used in otoneurological diagnosis do not appear to have been adopted for clinical research purposes as a result of these experiments.

Research into the measurement of the time of response has been going on since 1914 (Pierow); Chocholle studied this problem and published reports on the time of response at the appearance of a stimulus, upon variations of frequency and intensity, and then upon cessation of stimulus.

While considering the possibility of applying his research clinically, Chocholle nevertheless realized the many obstacles in the way of interpreting measurements, owing to their difficulty and the need for a large number of measurements for the same test, and the importance of individual variations.

Bocca and Matzker have studied the possibility of integrating elements of information by utilizing sentences (Bocca) or words (Matzker) as material. Bocca modifies the rhythm of the message and demonstrates that changes in the quality of a message certainly make it less possible for it to be repeated by the subject whose auditory cortical system is abnormal. Matzker utilizes two filters systematically (500-800 and 1815-2500 cycles): each filter permits the passage of a band which is sufficiently narrow to ensure that the word which is cut short in this way is unidentifiable; the two bands together, each of which is directed to one ear, should enable the word to be reconstituted sufficiently to make it intelligible provided that the integration of the two simultaneous different messages is correct.

Matzker considers that the lack of integration is the result of poor transmission of one of the components of the message, at least, when it is on its way to the cortex, and he asserts that he found there was no need to concern himself with the condition of the peripheral receivers.

From the assessments already made of these methods it may be seen that, according to statistics, in frequent cases it is an extremely delicate matter to interpret vocal tests utilizing filters, in otoneurological observations, with a progressive change of the threshold towards sharp frequencies: the analysis of the working parameters gives rise to doubts regarding the results of a test utilizing words which differ in fundamental vowels, and a voice which is not necessarily controlled in such a way as to guarantee the exactitude of the decreasing intensities in terms of time.

Vocal audiometry utilizes a process of audition which is concerned with both the centers of audition and those of language.

Disturbed responses to vocal tests may express an aphasis or an anarthric element, and the results depend on important elements in the intellectual level of the patient.

It may be desirable to deviate from the systemic attempts to utilize language for revealing, in particular, hearing troubles which may be due to lesions of the brain stem or to cortical lesions.

There may be grounds for taking the peripheral receiver (an obligatory passage) into account, and for directing research towards experiments which will enable a study to be made of a possible disturbance in the functioning of the relays or the integration.

In this sense, when faced with an unidentified syndrome, the observer does not know whether the attention paid to the auditory function should lead him to suspect a central lesion; consequently, the differential diagnosis should be based on an examination of the preliminary trace as well as a close investigation of the recruitment and an examination of the possibility of integration of the elements of information. In order to be able to make deductions from research into the possibility of recognizing a message, it is necessary for the message to be simple.

It is necessary to take the condition of the peripheral receiver into account; research into the effect of fatigue appears to be a good

means of acquiring knowledge and, in a simple form, this should constitute one of the subjects of the research as a whole. It is necessary to take into account the qualities of transference in the auditory passage: the "time" factor will therefore be another subject for research.

It is necessary to study the possibility of integration of the components of the message selected: the utilization of transitory phenomena, which is imperative and fundamental, presupposes a sure means of estimating the disproportion which exists between the weak energy level of the transients and the importance of their effects, due to the efficiency of the nervous system.

These three considerations lead to considerable importance being attached to the "time" factor in audiometric investigation. The tests which will be proposed should bring in a succession of transients separated by static conditions. And the operator should have a highly sensitive apparatus at his disposal, which makes it possible to analyze the temporal and spatial integration of the input which determines the sensation and preserves it in the memory.

AN EXPERIMENTAL IMPULSIVE AUDIOMETER

This apparatus is operated only through transients; it is designed in such a way as to permit the reproduction of the Bocca and Matzker tests, measurement of the time of response, and an unlimited series of new experiments.

Two pre-amplifiers A1-A2 may be connected to:

—either one or, separately, to two audio oscillators (BF), the frequency and intensity of which are adjustable;
—or to a microphone (M)

Simple noise generators may be substituted for the audio oscillators (BF).

The two pre-amplifiers are connected to two neon tubes N1-N2, which are placed above a disc in which holes have been pierced. Opposite the neon tubes, and under the disc are two electric cells, the current from which passes through the two output amplifiers A3-A4 to two ear-phones.

The contactor at the outlet C makes its possible to connect the two ear-phones in parallel or to separate them; in this case, each ear-phone is fed separately by one of the two amplifiers.

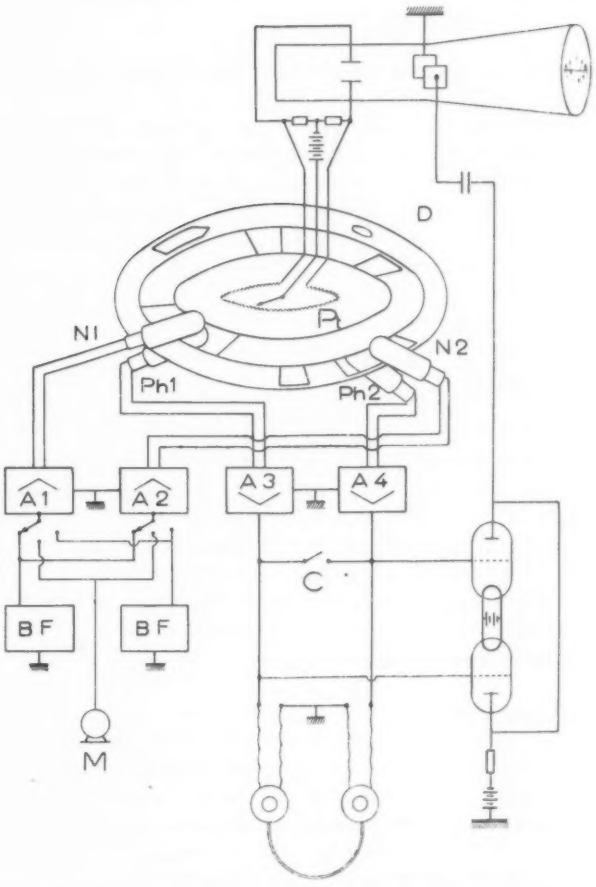

Fig. 1.—Experimental impulsional audiometer of Pimonow and Lucas.

A visual representation of the impulses applied to the subject's ear can be seen on a cathode-ray tube, the horizontal deviation of which is ensured by the potentionmeter P, mechanically coupled to a turntable, the vertical deviation of which is ensured by the voltage passing through the ear-phones.

The mounting-plate D is made of a transparent substance. The disc which covers the mounting-plate is interchangeable; it is made of

an opaque and flexible material, so that it is possible to cut windows in it, of a given shape and size.

The speed of the turntable may be varied, which makes it possible to regulate the duration of the impulses and the intervals of silence, whilst preserving the same ratio. Consequently, by changing the sources of stimuli, the speed of rotation of the mounting-plate and the discs, a wide series of combinations of transitory phenomena can be directed to one or both ears of a subject. The transitory phenomena may consist of either sinusoidal impulses or of the spoken word divided into sections, or of simple noise impulses.

Figure 1 is a skeleton diagram of this apparatus.

RESEARCH IN CONNECTION WITH AN IDENTIFICATION TEST

It may be of great clinical interest to investigate, by means of an identification test which does not demand the highest intellectual capacity, the differential diagnosis of a peripheral syndrome and a syndrome which may include a retro-cochleate element, i.e., a disturbance in the functioning of the relays or the integration.

It may be desirable to study the possibility of recognizing, in a precise and short space of time, a simple message composed of a weak and variable number of identical, grouped and brief stimuli.

To enable a subject to identify the number of stimuli, within a given time, he will need a variable amplitude in terms of the characteristics of the receiver, in terms of the transference qualities in the auditory passage, and in terms of the cortical function which determines the character of the message and expresses a response by stating a figure.

It appears necessary to produce these brief stimuli of variable intensity in an extended interval of silence which may separate intensive stimulations at equally spaced intervals, the dual purpose of which is to attract attention in this way to the silence which follows them, and to determine an effect of fatigue which takes into account the capacity for response of the receiver.

The experiments of Causse-Chavasse only lead to the selection of a frequency above 500 cycles; it may be preferable to utilize the same frequency for stimulation and for the signal. The work of Matthews leads to the supposition that the duration of stimulation should be

determined once and for all; a duration of one second may be suggested.

A constant amplitude should be selected for stimulation.

The establishment of an interval between stimulations is of the utmost importance in this experiment, and the notes made by Hood will serve for the preliminary investigation. It appears that the windows cut in the opaque disc of the apparatus, by means of which it is possible to establish an interval of silence of a very variable duration, as required by the observer, should be calculated in such a way as to ensure that the interval of silence is not less than 1600 milliseconds.

The duration of the stimuli of the same frequency as the intensive stimulation is also determined in advance by the size of the corresponding windows.

It appears that there should be a small number of these: one, two or three.

It appears that their duration should always be the same during the duration of a test, and should be lower, for the frequency selected, than the time necessary for appreciating the sensation of intensity.

CONCLUSION

The indispensable presence of transitory phenomena for the transmission of information leads to research on their use in experiments in an oto-neurological context.

The material submitted will lead to several series of new experiments which will contribute to the recognition of the importance of the "time" factor in the functioning of the hearing organ.

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THE DIAGNOSIS OF BRONCHOGENIC CARCINOMA

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Multiple diagnostic procedures are available for the investigation of patients with suspected bronchogenic carcinoma. The importance of bronchoscopic biopsy, anterior scalene lymph node biopsy, and needle biopsy of the lung has been well documented. More recently the cytologic examination of sputum, aspirated bronchial secretions, and pleural fluid has been found to be of practical value and is now widely used in the investigation of pulmonary lesions.

The purpose of this study was to determine the diagnostic accuracy and relative sensitivity of each of the diagnostic procedures used to establish the presence of bronchogenic carcinoma in a series of 482 proven cases.

METHOD AND MATERIAL

Between the period of 1951 to 1959, 482 patients were seen at the Temple University Medical Center where a histologic diagnosis of bronchogenic carcinoma was made. Patients with clinical evidence of lung cancer, but not confirmed histologically were excluded from this study. Also excluded were cases which were diagnosed prior to entering this hospital.

A bronchoscopic examination was performed at the Chevalier Jackson Clinic on 454 patients in this series. All bronchoscopies were performed under local anesthesia. Telescopic visualization of the tracheobronchial tree was routinely used.

In 376 cases, secretions were aspirated during the bronchoscopy and sent for cytologic study. Each specimen of secretion was smeared on four slides and prepared by the usual Papanicolaou technique for the cytologic examination.

Read in part to the Philadelphia Laryngologic Society on April 4, 1961.

There were 52 patients in whom one or more sputum specimens were examined for malignant cells. A single morning cough specimen was collected in a dry clean container and sent immediately to the pathology laboratory where four slides were prepared by the Papanicolaou technique from each specimen.

The results of the bronchial secretion and sputum examinations were reported in one of five classes as follows:

Class I	Negative
Class II	Presence of atypical cells
Class III	Suspicious of malignancy
Class IV	Fairly conclusive of malignancy
Class V	Conclusive of malignancy

Needle biopsy of the lung was performed in 117 cases. All needle biopsies were performed with a modified Franceen needle and a 30 cc syringe which was fitted with a ratchet lock to insure a partial vacuum in the syringe. A biplane fluoroscope was used to assist the surgeon in directing the biopsy needle to the tumor mass.

RESULTS

Bronchoscopy. A bronchoscopic examination was interpreted as positive only when a biopsy of bronchial tissue was obtained and its histologic examination revealed the presence of carcinoma. Bronchoscopic examinations were performed in 454 of the 482 cases. Carcinoma was demonstrated in 224 or 49.3% of those bronchoscoped.

Bronchial Cytology. Secretions were aspirated during the bronchoscopy and examined for the presence of malignant cells in 376 cases. The results of these cytologic examinations are presented in Table I.

The presence of Class IV or Class V cytology was interpreted as indicating the presence of malignancy in this series. It is shown that 38% of the bronchial secretions provided evidence of carcinoma (Class IV and V). In 15.7% of cases a suspicious (Class III) report was issued. In 46.3%, a relatively negative cytology was reported.

The combined results of bronchoscopic biopsy and bronchial secretion cytology were analyzed and presented in Table II.

TABLE I

CLASS DISTRIBUTION OF ASPIRATED BRONCHIAL SECRETIONS IN 376 CASES OF HISTOLOGICALLY PROVEN BRONCHOGENIC CARCINOMA

CYTOLOGIC CLASSIFICATION	NUMBER OF CASES	PERCENT
Class I	109	29.0
Class II	65	17.3
Class III	59	15.7
Class IV	51	13.5
Class V	92	24.5
	376	100 %

In the 376 patients who had the combined examination, 94 patients or 25% had both a positive bronchoscopic biopsy and a positive (Class IV or V) bronchial cytology. There were 65 cases or 17.3% in which the bronchial biopsy was positive but the cytologic examination did not reveal malignant cells. In 49 cases or 13%, tumor was not visualized endoscopically, but malignant cells were identified in the aspirated bronchial secretions. In 168 cases or 44.7%, both the bronchoscopy and the bronchial cytology were unrevealing. When combining bronchoscopy with the cytologic examination of aspirated secretions, a positive diagnosis was obtained in 55.3% of cases.

Needle Biopsy of Lung. Needle biopsy of the lung was performed with the aid of biplane fluoroscopic guidance in 117 cases. In 83 cases (70.9%) the tissue obtained revealed the presence of carcinoma. Thirty-four biopsies (29.1%) were negative. This procedure established the tissue diagnosis of carcinoma in 69 cases, whereas in 14 cases it confirmed the diagnosis which had been established by prior bronchoscopic biopsy or cytology.

Scalene Node Biopsy. The scalene node biopsy was utilized to establish histologic evidence of bronchogenic carcinoma as well as to aid in determining the operability of the patients. In this series, the scalene fat pad with its contained lymph nodes was excised in 81 patients. Carcinoma was present in 42 (51.9%) of these specimens. This procedure confirmed the suspected diagnosis of bronchogenic

TABLE II

COMPARATIVE RESULTS OF BRONCHOSCOPY AND BRONCHIAL CYTOLOGY

CLASSIFICATION	NUMBER OF CASES	PERCENT
Bronchoscopy positive with Class IV cytology	30	8.0
Bronchoscopy positive with Class V cytology	64	17.0
Bronchoscopy positive with negative cytology	65	17.3
Bronchoscopy negative with Class IV cytology	21	5.6
Bronchoscopy negative with Class V cytology	28	7.4
Bronchoscopy negative with negative cytology	168	44.7

carcinoma in 20 patients, and it was an aid in determining the operability in 22 additional cases where the diagnosis had already been proven.

Pleural Fluid Cytology. Thoracentesis with the examination of the pleural fluid for the presence of malignant cells was performed in 32 patients on one or more occasions. In 7 cases the pleural fluid did not reveal the presence of malignant cells, while in the remaining 25 cases, malignant cells were identified. Histologic evidence of malignancy was supplied by this procedure in 16 cases, while in the other 9 cases, the diagnosis had been established by prior bronchoscopic biopsy.

Biopsy of Metastatic Lesions. In 18 cases a positive biopsy of a metastatic lesion was obtained. This tissue was the only histologic evidence of pulmonary malignancy in 12 patients who had both clinical and x-ray evidence of bronchogenic carcinoma. In the remaining 6 cases, histologic evidence of pulmonary malignancy had been obtained by a prior procedure. Table III lists the sites from which these biopsies were obtained.

Sputum Cytology. During the latter part of 1958, the examination of sputum for cytologic evidence of malignancy was undertaken by the Department of Pathology. In the present series, 52 patients had one or more sputum specimens examined for the presence of malignant cells. The sputum was positive (Class IV or V) in 40 cases or 77%. Sixteen cases were Class IV and 24 were Class V.

TABLE III

SITES FROM WHICH BIOPSY OF METASTATIC PULMONARY LESION WAS OBTAINED

SITE	NUMBER OF CASES
Chest Nodule	3
Ribs	3
Femur	2
Scapula	2
Pleura	2
Brain	2
Clavicle	1
Sacrum	1
Liver	1
Bone Marrow	1
	18

TABLE IV

COMPARATIVE RESULTS OF BRONCHOSCOPY AND SPUTUM CYTOLOGY

	SPUTUM CYTOLOGY	
	POSITIVE	NEGATIVE
Bronchoscopic Biopsy and/or Bronchial Cytology positive	24	7
Bronchoscopy with Bronchial Cytology negative	11	5
Bronchoscopy not performed	5	0

TABLE V

ACCURACY OF DIAGNOSTIC PROCEDURES IN THE PROVEN CASES OF BRONCHOGENIC CARCINOMA

PROCEDURE	NO. EXAMINED	NO. POSITIVE	PERCENT
Bronchoscopy	454	224	49.3
Bronchial Cytology	376	143	38.0
Bronchoscopy with Bronchial Cytology	376	208	55.3
Needle Biopsy of Lung	117	83	70.9
Scalene Node Biopsy	81	42	51.9
Sputum Cytology	52	40	77.0
Pleural Fluid Cytology	32	25	78.1

Table IV illustrates the comparative results of bronchoscopy and sputum cytology in these cases.

It will be noted that in 24 cases, both the bronchoscopy and sputum cytology were positive. In 11 cases, the sputum cytology was positive, while the bronchoscopy and bronchial cytology were unrevealing. In 7 cases, the bronchoscopy was positive but no malignant cells were demonstrated in the sputum specimens. There were 5 cases in which both bronchoscopy and sputum examinations did not reveal the presence of malignancy. Five patients had positive sputum specimens but were not bronchoscoped.

Thoracotomy. Despite the use of the various diagnostic procedures, 75 (15.6%) of the 482 cases were undiagnosed histologically until thoracotomy was performed.

Autopsy. One patient who had a negative bronchoscopy and bronchial cytology expired a few days following his admission and at autopsy a large bronchogenic carcinoma with multiple metastasis was found.

The accuracy of the various diagnostic procedures is summarized in Table V.

A positive biopsy was obtained in 49.3% of those bronchoscoped. Malignant cells were identified in 38% of the aspirated bronchial

TABLE VI

DEFINITIVE DIAGNOSTIC PROCEDURE IN THE 482 CASES OF BRONCHOGENIC CARCINOMA

	NUMBER OF CASES
Bronchoscopic Biopsy	224
Bronchial Cytology	49
Needle Biopsy	69
Scalene Node Biopsy	20
Sputum Cytology	16
Pleural Fluid Cytology	16
Biopsy of Metastatic Site	12
Exploratory Thoracotomy	75
Autopsy	1
	482

secretions. When bronchoscopy is combined with the cytologic examination of the aspirated secretions, a positive diagnosis was made in 55.3% of the patients. Needle biopsy, scalene node biopsy and pleural fluid examinations all yield a high percentage of positive results, although they are indicated less frequently then the bronchoscopic procedures. Sputum cytology was positive in a high percentage of cases, and proved to be a valuable addition to the investigation of pulmonary malignancy.

The comparative frequency by which each of the diagnostic procedures established the presence of bronchogenic carcinoma in the 482 cases is presented in Table VI.

Bronchoscopic biopsy established the diagnosis of carcinoma in 224 cases. Bronchial cytology revealed the diagnosis in 49 cases. Needle biopsy proved to be an effective diagnostic procedure especially in the peripherally located tumors, and accounted for the diagnosis in 69 cases. Scalene node biopsy, sputum cytology, pleural fluid cytology, and biopsy of metastatic lesions were all of diagnostic aid, but in a smaller number of cases. Although multiple diagnostic methods were available, 75 cases were undiagnosed prior to thoracotomy.

COMMENT

The value of bronchoscopy in the early suspected cases of pulmonary malignancy has been repeatedly stressed.[1-4] A positive diagnosis by means of bronchoscopic biopsy has been reported in from 26 to 60 percent of patients with bronchogenic carcinoma.[5-7] In the present series, bronchoscopic biopsy was positive in 49.3% of the cases. As a method of direct inspection which can be carried out with minimal discomfort and risk to the patient, bronchoscopy provides a great deal of information. Besides the biopsy of growths in the accessible bronchi, the secondary effects of a lesion on the bronchial tree is revealed, such as deformity, compression, rigidity, and displacement. Although the amount of peripheral infiltration cannot be determined by bronchoscopy, its proximal extent is readily observed. Gross infiltration of the carina, a dilated or fixed carina, and the lack of mobility of the vocal cords provide valuable information to the surgeon regarding the extent of the lesion and its resectability. Even though the carina may appear normal, a paracarinal biopsy as advocated by Rabin,[8] may demonstrate the presence of submucosal lymphatic spread of the tumor.

The cytologic study of bronchial secretions aspirated at the time of the initial bronchoscopy has made possible the detection of malignancy which is beyond the range of bronchoscopic visualization in a significant number of cases, thus further increasing the value of bronchoscopy. McKay[9] was able to demonstrate the presence of malignancy by cytologic smear of aspirated bronchial secretions in 26% of patients who had no tumor visible by bronchoscopic inspection. Other reports[10,11] indicate that the addition of this cytologic examination has allowed an additional 20 to 30% of patients to be diagnosed by bronchoscopy. Bronchial cytology increased the detection of malignancy by the bronchoscopic procedure by an increment of 13% in the presently reported series.

The examination of sputum for the presence of malignant cells has proven to be a useful adjunct in the diagnosis of pulmonary malignancy. Since expectoration of sputum is commonly present in patients with bronchogenic carcinoma, the material is readily available for pathologic study and multiple daily specimens may be obtained for examination. Tassoni[12] was able to show that the diagnostic accuracy of the first sputum specimen was 51.9% while that of the first bronchial aspirate was 42.6%. When multiple sputum specimens are examined, the accuracy of sputum cytology increases. Farber[13] has reported a 90% accuracy in the diagnosis of lung cancer when five or more sputum specimens were examined. The efficiency of this

cytologic method has been attested by many investigators, with the accuracy of diagnosis ranging from 75 to 90 per cent in various published series.[14-17] Although only 52 of our patients had sputum examinations, 77% were found to be positive (Class IV or V).

The technique of removing the anterior scalene lymph nodes and its merits in diagnosing intrathoracic disease was first demonstrated by Daniels in 1949.[18] This procedure has a two-fold purpose; the histologic confirmation of the presence of a malignant tumor, and the determination of surgical curability. When nodes are not palpable, the site of the primary lesion determines the choice of the site for biopsy. In general, the right lung and the left lower lobe drain into the nodes of the right cervical area, while the left upper lobe drains into the left cervical area. Cross drainage is not uncommon. If nodes are palpable, it is best to perform a biopsy of these regardless of the site of the lesion. Shapiro[19] demonstrated positive nodes in 19% of his cases. In the instances of non-palpable nodes, the incidence was 8.1%. Umiker[20] reported 24% of his cases had positive scalene nodes, while Shefts[21] reported metastatic neoplasm in the scalene nodes of 54.2% of his patients with primary bronchogenic carcinoma. Metastatic neoplasm was found in 51.9% of the 81 patients selected for this procedure by our surgical staff.

Some controversy still exists as to the value of needle biopsy in the lung lesions considered to be operable. Several authors[22-26] have stated that needle biopsy should be reserved for only those cases in which other diagnostic aids have failed to establish the diagnosis in an inoperable malignant lesion. The role of needle biopsy in such cases is to supply the tissue diagnosis that must be obtained before rational palliative measures such as irradiation or chemotherapy can be initiated. They further state that if evidence suggests that the lesion is operable, then needle biopsy should be bypassed and thoracotomy with the appropriate resection performed, since a negative needle biopsy would not rule out the presence of malignancy and a positive biopsy would still make thoracotomy mandatory. The needle biopsy in operable lesions thus being considered superfluous and adding the risk of implanting tumor cells in the chest wall.

At our institution, Burnett, Rosemond, and Lauby[27-30] consider needle biopsy to be of definite value in operable pulmonary lesions that remain undiagnosed after complete study by the conventional methods. They feel that if the diagnosis is to be made by thoracotomy, the following problems arise:

a. Incision frequently must be made directly into the tumor for a specimen, with resultant contamination of the pleural space with viable tumor cells.

b. Frequently several incisional biopsies must be made before representative tissue is obtained.

c. Removal of hilar lymph nodes as a biopsy specimen interrupts the enbloc operation for cancer.

These problems would be avoided by a positive needle biopsy and the surgeon could proceed with the definitive operation. Burnett[31] has found no case of implantation of tumor cells along the needle tract in over 20 years' experience with this procedure.

SUMMARY

An analysis of 482 proven cases of bronchogenic carcinoma was presented with respect to the manner in which the definitive diagnosis was established. The diagnostic procedures were evaluated and their accuracy and relative sensitivity reported.

The present presentation reveals the fact that no single procedure can be relied upon to establish the presence of pulmonary malignancy. However, bronchoscopy combined with the cytologic examination of the aspirated secretions was found to produce the greatest number of positive tissue diagnoses.

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LI

FRACTURE OF AN ELONGATED STYLOID PROCESS MASQUERADING AS A FOREIGN BODY

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An endoscopist may find fracture of the styloid process providing a surprising diagnostic challenge. Most are aware that the x-ray appearance of a normal or elongated styloid process can be mistaken for a foreign body. A fractured styloid can create very confusing clinical and x-ray findings.

Probably the earliest reference to the clinical problem of elongation of the styloid process is Lücke's[1] report in 1870, although anatomists were aware of this variation as early as 1652 when Marchettis[2] commented on it. In his drawing of the hyoid bone published in 1543, Vesalius[3] sketched what appears to be elongated styloid processes. However, he may have been influenced by animal specimens which he occasionally substituted for human.

In 1896, Stirling[4] described three patients with persistent throat pain and a palpable mass in the tonsillar area. He concluded that the symptoms and findings were due to abnormal elongation of the styloid process and pointed out the potential hazard of careless tonsil surgery in such individuals.

Thigpen[5] discussed the surgical treatment of symptomatic elongation of the styloid process in 1932. In his first patients, he removed the elongated or angulated portion of the process. Later, he found that fracturing of the process would relieve the patient of his symptoms. These latter cases are the first reported cases of fracture of the styloid process.

Fritz[6] reported 43 cases of elongated styloid process in 1940. He discussed the symptomatology in detail, stressing glossopharyngeal nerve neuralgia.

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In 1945, Sinberg and Burman[7] reported two cases of fracture of the styloid process. The first was a 30 year old man whose jaw had been dislocated by a blow on his head. X-rays showed a fracture of the styloid process. The second patient was a 60 year old man who had sustained multiple fractures in an automobile accident. He had what was interpreted as a fracture of the styloid process, although the authors raised the possibility that his x-ray findings could represent a normal variation . . . the "bipartite" styloid process.

Equen mentioned a patient with a fractured styloid process in a discussion of a paper by Eagle.[8] He saw a 45 year old woman who had suffered a fracture of the styloid process during oral surgery when she "jumped around in the dental chair." He removed the fractured portion by an approach through the tonsillar fossa.

REPORT OF A CASE

A 23 year old soldier was admitted to Ireland Army Hospital with the chief complaint of "a bone sticking in the throat." A few hours prior to admission he had choked while eating a pork chop, and the sensation of a foreign body had persisted in spite of his efforts to dislodge it by eating bread and by inducing emesis.

Palpation revealed a sharp, bony mass in the region of the left pharyngeal epiglottic fold. No foreign body was seen upon indirect laryngoscopy, so a direct laryngoscopy was performed with the confident assumption that it would be revealed. Gagging and restlessness prevented a thorough examination of the hypopharynx under local anesthesia, and no foreign body was seen.

The patient was then scheduled for an examination under general anesthesia. Pre-operative x-rays were interpreted as showing a foreign body in the hypopharynx (Fig. 1).

Laryngoscopy and esophagoscopy were performed under general anesthesia with an endotracheal tube in place. No foreign body was visualized. However, palpation made it evident that the bony abnormality in the left lateral hypopharynx was attached to the hyoid bone and that it was entirely submucosal. Re-evaluation of the x-ray findings led to the conclusion that it represented a fracture of an elongated styloid process.

It was felt that surgical removal of the fragment was not indicated, and the patient was observed carefully for a period of six

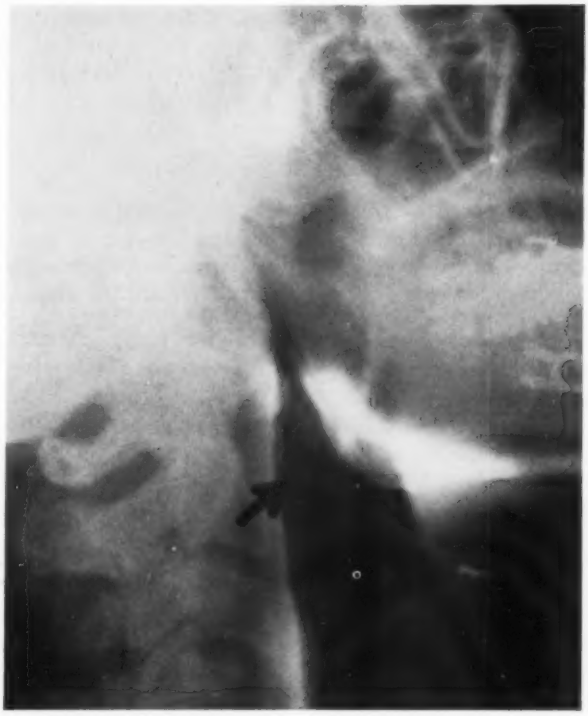

Fig. 1.—X-ray view showing fracture of the elongated styloid process.

months. During this time, his symptoms cleared up, but the mass remained palpable.

COMMENT

The fracture of the elongated styloid process probably occurred when the patient choked on a piece of meat. Another possibility is that his violent efforts to dislodge a foreign body were successful, but also fractured the bone. However, pre-existence of the condition cannot be ruled out.

If I had been aware of this entity when I first saw the patient, the proper diagnosis could have been suspected. The x-ray findings are similar to those that have been previously published.

Although the hazard of a sharp fragment of bone in the region of the great vessels of the neck was considered, and Equen had reported removal of a fractured styloid process, it did not seem necessary to submit the patient to further exploration for removal of the bone. During the follow-up period, he quickly became asymptomatic, and remained so for six months.

SUMMARY AND CONCLUSIONS

Fracture of an elongated styloid process was observed in a 23 year old man. His history and findings first led to the mistaken diagnosis of a foreign body. Only palpation under general anesthesia with consideration of the x-ray findings corrected the diagnosis.

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LII

ON FOREIGN BODIES, PERI-ESOPHAGITIS AND COLLAR MEDIASTINOTOMY

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In 1953 the experience of the clinic in Groningen with foreign bodies in the esophagus was described in this journal.[1] It was mentioned that after the last war we saw an increasing number of foreign bodies in the esophagus, in the first place, fish bones. It is a remarkable fact that the war has changed the number and the kind of the foreign bodies in the esophagus. The difference is very striking here. The increase of the number of foreign bodies in the esophagus had already started during the war. Meat was scarce and that was the reason that people began to eat more fish, which was continued after the war. Other reasons for this increase have been mentioned in the first paper: 1) the patients are directed to the clinic by the doctors sooner than formerly; 2) perhaps people eat more carelessly in these hurried times; 3) there are more people with false teeth, who swallow fishbones and also other foreign bodies more easily.

It is interesting to ascertain that even in foreign bodies in the esophagus we depend on the external circumstances, and to see the change by the war in the north of this country:

In 33 years before the war:	148 foreign bodies	8 fishbones
In the 6 years during the war:	87 foreign bodies	34 fishbones
In the 15 years after the war:	371 foreign bodies	122 fishbones

In the northern part of the Netherlands the fishbone is now foreign body No. 1 in the lower food and air passages. Before the war foreign body No. 1 was peanuts, which were aspirated by many children. During the war we had not one single case of aspiration of a peanut; since the war these cases are relatively rare. This was the reason for a large decrease of the number of foreign bodies in the bronchi after the war. There is an enormous change as is shown in the following statistics, which compare the number of foreign bodies in

the bronchi and in the esophagus during the six years before the war with those of the last six years.

		Number of Foreign Bodies
Bronchi	1934-1939	117
	1955-1960	46
Esophagus	1934-1939	49
	1955-1960	160

As a sequel to the previous paper the following statistics are given: We saw 210 patients with a foreign body in the esophagus in the clinic in these last nine years. An external operation, a collar mediastinotomy was necessary in four patients. One patient died.

REPORT OF CASES

CASE 1. A man, 45 years of age, swallowed a chicken bone. He came in the clinic a few hours later, with much pain in the neck and behind the sternum, vomiting blood. There was no foreign body or emphysema on a lateral roentgenogram of the neck. Esophagoscopy showed severe lesion of the esophagus, probably a perforation; there was no foreign body. He had so much pain in the thorax and the general condition was so alarming that the same evening first a thoracotomy (Prof. *Eerland*) was done; there was food in the mediastinum, drainage. Collar mediastinotomy was performed, with exposure of a tear in the esophagus, and closure. The first weeks it seemed that the patient would recover, but later he had much trouble with diuresis and he died two and a half months after the operation from uremia. Thus, in the only case in many years of a patient who died from swallowing a foreign body, this was not the direct reason. This was the only death in a continuous series of 600 foreign bodies in the esophagus, a remarkable difference with the earlier years of esophagoscopy.

A fact worth noticing (but our experience is not so large) is that in the only death an external operation was done a few hours after the perforation of the esophagus. As was discussed already in the previous paper, a perforation of the esophagus in itself is not yet an indication for operation. We saw several patients with a perforation, who recovered without an operation, under treatment with antibiotics. The collar mediastinotomy is now a rare operation. It is only by pure

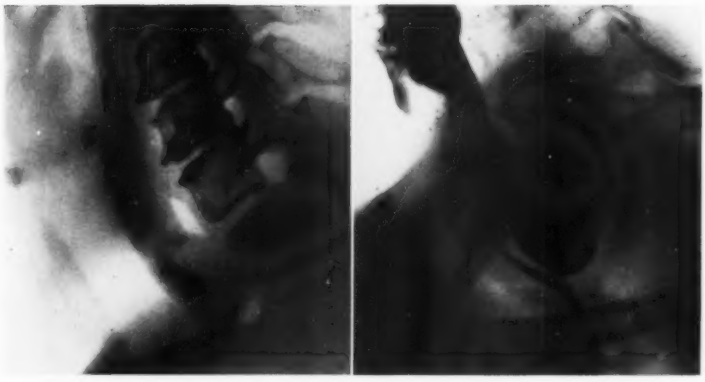

Fig. 1.—Case 2.

coincidence that in 1957 we performed this operation on four patients. Two patients had a perforation caused by a foreign body; in the two others an esophagoscopy was the cause. All patients recovered; two patients are described later as Cases 3 and 4.

We are, as a rule, conservative in our treatment in a perforation of the esophagus. The patients are fed by intravenous infusion during the first days and large doses of antibiotics are given. Very important is a regular checking by the radiologist.

In the previous paper we have described the great value of x-ray examination of the neck with lateral films, in patients with a possibility of a perforation of the esophagus. By diagnosing air in the tissues of the neck a perforation of the esophagus can be ascertained. We discussed the symptom of Minnigerode[2]: the emphysema of the interstitial tissue in the neck, as a sure sign that the esophagus has been perforated, and one or more big air-bubbles which often indicate the presence of an abscess.

We have mentioned previously[1] the possibility of a misunderstanding when in the case of a foreign body in the esophagus some small air-bubbles are adhering to the object between the folds of the swollen mucous membrane. It was described in Figure 1 under diagram 1a in the previous paper.

Fig. 2.—Case 3.

In a paper with Keyser[3] we recorded another pitfall: sometimes an air-bubble passes the esophagus in swallowing, also in normal persons. It is possible that the radiologist shot the photograph at that very moment. The result is that there is an air-bubble between the trachea and the spine. Lately we saw the same picture in a patient with a diverticulum of Zenker of the hypopharynx.

CASE 2. A man, 58 years of age, had complaints of swallowing, regurgitation and particular noises in his throat during the last year. Figure 1 left is the lateral photograph of the neck and Figure 1 right

Fig. 3.—Case 4.

is of the same patient after swallowing barium. In the left hand picture an air-bubble can be seen, outlined below by a sharp clear line, obviously a fluid level. The one on the right makes it clear that it is air and fluid in a diverticulum. The roentgenogram of Figure 1 left alone may be misleading; the picture has a great resemblance to a picture of a peri-esophageal abscess. In a peri-esophagitis the distance between the trachea and the vertebral spine is larger than normal. This swelling of the peri-esophageal tissue is an important symptom and can be seen on a lateral roentgenogram. We see in Figure 1 that through the diverticulum this distance is too large.

Fig. 4.—Case 5. Right, 36 days later.

In this figure there is a second place where air can be seen between trachea and vertebral spine lower than the air-bubble in the diverticulum. This is the dome of the pleura, another possibility for misunderstanding.

For the presence of air in the peri-esophageal tissue there are two possibilities: 1) it may be air sucked in through the perforation (emphysema) or 2) gas is formed by certain bacteria. In an acute case with a fresh perforation we always see an emphysema of the interstitial tissue of the neck. We mostly see a light streak in front of the spine, but several times we found air in other parts of the neck. It is well known that in these cases it can be felt at the neck. Seiffert[4] in one of his short and excellent papers has already drawn attention to the fact that the presence of air was solely the result of the esophagoscopy. Normally the esophagus is closed and contains no air. Above we mentioned the air-bubble by swallowing but this is an exception in normal adults. Aerophagia in large quantities is rare but well known, and it is always considered to be pathological. But as soon as the mouth of the esophagus is opened by the esophagoscope we see that there is air in the thoracic esophagus, which shows the typical movement of the walls in breathing. Now when there is a perforation, the air can be sucked in by the negative thoracic pressure during

Fig. 5.—Case 5. Left, bilateral collar mediastinotomy; right, 13 years later.

inspiration. In a short time large quantities of air can enter the peri-esophageal tissue. We describe the following patient, because the x-ray of the emphysema in this case was very demonstrative.

CASE 3. A man, 65 years of age, eating soup swallowed a small bone. He had much pain in the neck. After three hours he came to the clinic. A lateral roentgenogram of the neck showed no abnormalities; there was no shadow of a foreign body and no emphysema. Esophagoscopy was done very carefully, a circumscribed deep lesion, ± 1 cm long, was found in the lower part of the mouth of the esophagus. The impression was that there could be a perforation of the wall; there was no foreign body but the lesion and the anamnesis made it certain that a foreign body had been in the mouth of the esophagus. The patient was fed by intravenous infusion the first days, antibiotics were given. Figure 2 is the lateral roentgenogram of the neck, which was taken the next day. It is a striking picture of emphysema of the neck, which could also be felt by palpation. Treatment with antibiotics (2.000.000 U penicillin and 1 gram streptomycin) continued under regular x-ray control of the neck. The patient had a very severe asthma, he was operated upon on the ninth day under ACTH. A collar mediastinotomy was done because the x-ray demonstrated an abscess which was found at the operation. Recovery.

CASE 4. Figure 3 is the lateral roentgenogram of a woman of 74 years of age. It is a typical example of the second possibility, the large bubble here is gas formed in a peri-esophageal abscess. The

Fig. 6.—Case 5. 13 years later.

outline below is a sharp clear horizontal line, characteristic for a fluid level. In this woman an esophagoscopy was done eight days previously. She had a thoracic diverticulum. The esophagoscopy was difficult and a lesion in the mouth of the esophagus was caused. The lesion seemed to be very superficial, she was in excellent condition after the endoscopy, so she went home. Here she had some pain and after some days she had trouble in swallowing, the last day it was impossible for her to eat any food.

The roentgenogram, Figure 3, was taken when she came in the clinic, and gave the indication for immediate operation, collar medi-

astinotomy with drainage of an enormous abscess with foul stinking pus. She recovered very quickly. It is interesting that such a large abscess was found a short time after a small innocent looking lesion of the esophagus. In inspecting the esophagus during the collar mediastinotomy no lesion of the esophagus was found. The diagnosis was made: peri-esophageal infection, probably lymphatic, through a superficial esophageal lesion. In the lateral roentgenogram, Figure 3, we see a marked arthrosis of the cervical spinal column, especially of C VII, just at the place of the mouth of the esophagus. It is possible that the protrusion of C VII was the cause of the lesion.

The reason why we are coming back to collar mediastinotomy is that about the same time we saw again a German soldier, whom we had treated during the occupation of Holland in 1945.

CASE 5. A soldier, 22 years old, came into the clinic February 13, 1945, with a wound at the right side of the neck, about 5 cm long. On February 2 a splinter of shrapnel had hit him. The splinter was removed by a surgeon and the wound was closed with the exception of a small opening at the lower end; there was no drainage. The wound was opened again on February 17 because the patient had pain and a swelling developed. There was a lesion of the hypopharynx in the right sinus piriformis and, by pressing, air escaped. There was drainage. The patient went on complaining of pain; there was no temperature. A lateral roentgenogram of the neck showed no abnormalities. There was no swelling of the prevertebral tissue, no emphysema, the vertebrae were normal (Fig. 4, left). After consultation with the neurologist we considered the complaint as functional and he went over to the neurological department. The pain in the shoulders and in the neck became worse after a few weeks, the temperature went up to 38.6° C. We were much surprised when we saw a new lateral roentgenogram of the neck taken on March 22 (Fig. 4, right). There was a swelling of the prevertebral tissue and destruction of the vertebrae C V and especially C VI. We performed a collar mediastinotomy, there were granulations and some pus in the peri-esophageal tissue. There was an arrosion of the bodies of vertebrae V and VI and rough bone could be felt. Fixation of the neck in plaster was done.

March 28. The temperature was normal again, but the patient complained of more pain. Some days later the neurologist found symptoms of a transverse lesion of the medulla and disturbance of the sensibility, at the right side Babinski and clonus of the foot.

April 12. Collar mediastinotomy was done also on the left side to give maximal drainage of the prevertebral tissues. Here again there was much granulation (microscopy: inflammation tissue) and some pus. Figure 5 shows the patient with drains from the right to the left side in front of the vertebral spine behind the esophagus.

When our Canadian friends came to Groningen in April 1945, they, immediately on April 22, evacuated the German patients from the University Hospital in Groningen; this patient went away under my protest. He had a paresis of both legs, a typical Brown-Séquard myelitis transversus. His neck, of course, was in plaster, but with this spondylitis and with severe neurological symptoms, I had the idea that a transport to Germany would cause his death. I was much surprised to see him back after so many years in very good health. After the evacuation he had been in a hospital in Germany for many months; recovery came very slowly. Figure 5, right, shows the scars in the neck and Figure 6 is a lateral roentgenogram, which shows an ossification of the vertebrae C V, C VI, C VII, which are grown together.

It was a mistake to make a closure of the wound without drainage and without exposure of the lesion at the bottom of the right sinus piriformis. Probably this was not noticed. The peri-esophagitis took an unusual, chronic course. A spondylitis as a complication of a peri-esophagitis is a very rare complication, I could not find it in the literature.

The last case taught us a very good lesson, we have made the mistake of attaching too great a value to the normal roentgenogram of Figure 4. The lateral x-ray of the neck can give much information in these patients but Figure 4 demonstrates that a normal roentgenogram is no certain proof that there is no inflammation in the peri-esophageal tissue. But this often is the case in x-ray examination in general. A positive result is a certain indication but a negative x-ray examination does not mean that there is no lesion. With the complaints of the soldier, of course, a second roentgenogram was indicated much earlier, but at that time x-ray material was scarce. So in reality this case demonstrates again that in these patients regular x-ray checking is necessary.

SUMMARY

1. Statistics of foreign bodies in the esophagus, from the Groningen University Clinic, are given.

2. The symptom of Minnigerode, emphysema or an air-bubble found in x-ray examination of the neck with lateral films are discussed.

3. Some patients on whom a collar mediastinotomy was performed are also discussed.

4. This paper is a sequel to a paper on the same subject[1] in this journal in 1953.

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LIII

HEALING OF STAPEDIAL FRACTURES

OBSERVATIONS ON TISSUE CULTURE WITH THE TANTALUM EAR CHAMBER IN RABBITS

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AND

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Since the introduction of the mobilization technique for the restoration of hearing by Rosen[13] in 1953, surgical interest has centered on the problems of histologic repair after the therapeutic separation of the stapes, or parts of its footplate, from the ankylosing otosclerotic focus. If mobilization is to be successful, the stapes or its mobilized segments must remain freely movable without subsequent re-fixation by callus formation or otosclerotic regrowth. The complexities of this question are readily apparent from the large number of recent contributions to the problem of mobilization and to the various modifications in technique.

As an initial stage of a research program devoted to some basic problems of middle ear surgery, we decided to investigate the histologic behavior of the stapes following various surgical interventions on this bone in animals. The first question was the mode of repair in a fractured footplate of the rabbit stapes. Dr. Harry P. Schenck suggested the tissue culture technique by means of the tantalum chamber inserted into the rabbit ear lobe. This technique has proved its value for various problems of tissue culture in vivo.[15,16] One of us (Choo) studied the technical details with Dr. R. G. Williams in Philadelphia.

The tantalum chamber technique (Fig. 1) offers the following advantages: 1) it represents an in vivo tissue culture; 2) the chamber

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This study was aided by the John A. Hartford Foundation, Inc., of New York.

can be examined under the microscope without any preparation which permits daily observation; 3) microphotographs in vivo can be obtained whenever desired; 4) at the end of the animal's life the specimen is available for histologic study. These possibilities were explored for two purposes: one, to define the value of the tantalum chamber for ear research in general; and two, to study tissue repair in a fractured stapes as a first specific question.

Several authors[6,10,11] observed that fractures of the human stapedial footplate may heal by fibrous union. Similar opinions were voiced by previous authors quoted in those papers. This peculiarity is usually explained by the characteristic histologic structure of the labyrinth capsule. Nager[12] noted bony union of a fracture in the periosteal layer of the labyrinth capsule, whereas in its enchondral layer the persistent fissure contained only connective tissue. Hallpike[9] described the histologic changes found in a case of deaf-mutism which included a transverse fracture of the temporal bone that had healed by fibrous union.

In contrast, Bellucci and Wolff[4] stated that fractures of the stapes in cats and monkeys are usually united by accretion of new bone regardless of the fracture site. Altmann and Basek[2] studied experimental fractures of the stapes in rabbits and saw bony reunion of the footplate fragments in seven out of fifteen fractured stapes bones. Burton and Lawrence[7] used tissue culture methods to observe osteoblastic activity in the fractured footplate and crura of guinea pigs and of two human specimens. They found an osteogenic layer of dormant osteoblasts along the surface of the stapes. These osteoblasts respond to a stimulus, such as by a fracture, and carry out the repair process similar to that found in bone elsewhere in the body.

TECHNIQUE OF CHAMBER INSTALLATION AND TRANSPLANTATION OF BONE

The technique of inserting a tantalum chamber into the rabbit ear lobe was described by Williams and Roberts[14] in 1950. Our present project deals with autografts of stapes footplate in this particular rabbit race. In order to guard against possible damage to the chamber, the stapes from the opposite ear was used as implant (Figs. 2 and 3).

Two to three months after insertion of the chamber, i.e., at a time when the chamber is well vascularized, the rabbits were anesthetized with Nembutal® supplemented with local anesthetics (Xylo-

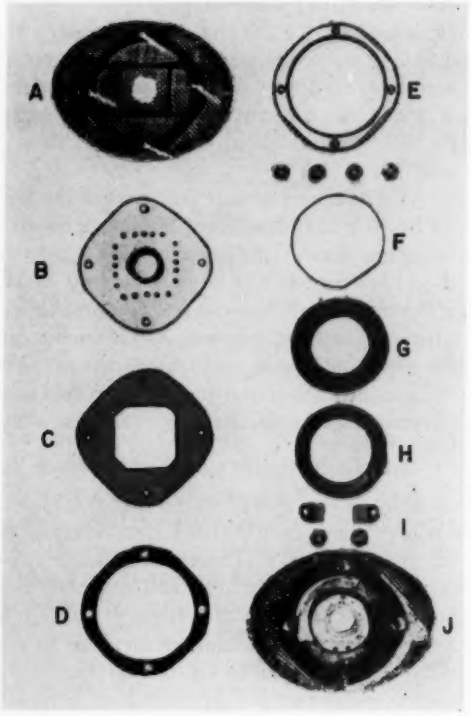

Fig. 1.—Assembled ear chamber (J) and its component parts (A-I). Courtesy, Williams and Roberts, Anat. Record 107:359, 1950.

cain®). After elevation of the soft tissues and ear drum, the long process of the incus was pushed forward by severing its joint which exposed the stapes. Following section of the stapedial tendon, the stapes was removed from the oval window and immersed immediately into Tyrode solution at 4° C.

Under the operating microscope, both crura were removed from the footplate which was then sliced to the desired size with a sharp knife. Since the periphery of the footplate is thick (250 micron anteriorly and 420 micron posteriorly[5]), its thin central portion (42-75 micron[1]) was chosen for our present work. Great care was taken not to damage the covering mucosa including its periosteum and end-

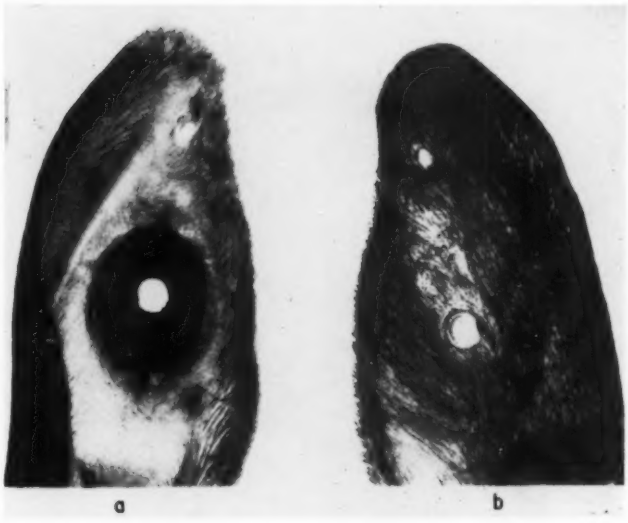

Fig. 2.—Rabbit ear lobe with chamber in place; a) inner surface, b) outer surface. Courtesy, Williams and Roberts, Anat. Record 107:359, 1950.

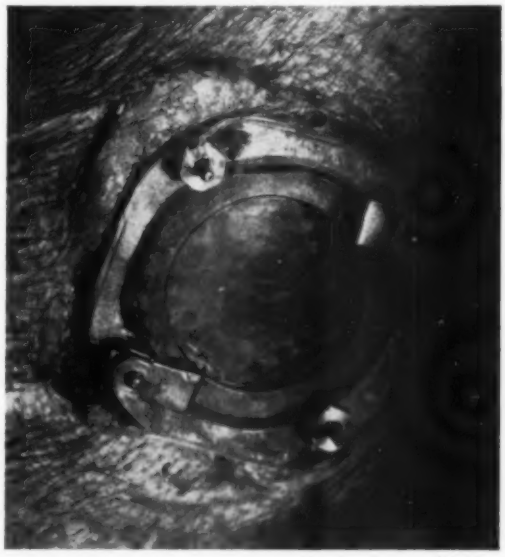

Fig. 3.—Enlarged view (2x) of Figure 2a. A fairly large blood vessel is seen in the left side of chamber.

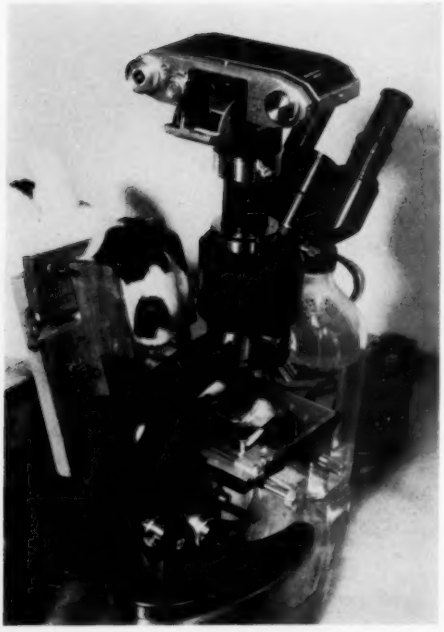

Fig. 4.—Observation of chamber. Without anesthesia the rabbit is fixed in a holder so that the ear lobe with the chamber is placed under the microscope for simple and photographic observation. Note water cooler for prevention of heat damage to chamber.

osteum. It is believed that the presence of these membranes is important for the survival of implanted bone.

As soon as the footplate is ready for transplantation, the ear lobe with the chamber is fastened to the stage of the microscope. The well of the chamber is cleaned with Metaphen® or Zephirin,® rinsed with Ringer's solution, and finally filled with Tyrode solution. After opening the screws, the mica cover is lifted and the pieces of bone previously prepared are now transplanted. Finally, the chamber is sealed again by replacing the cover and its accessories. From then on, microscopic observation of the implants is carried out whenever desired (Fig. 4).

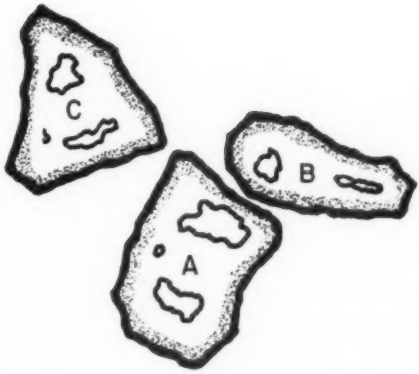

Fig. 5.—Schematic outline of three newly transplanted fragments.

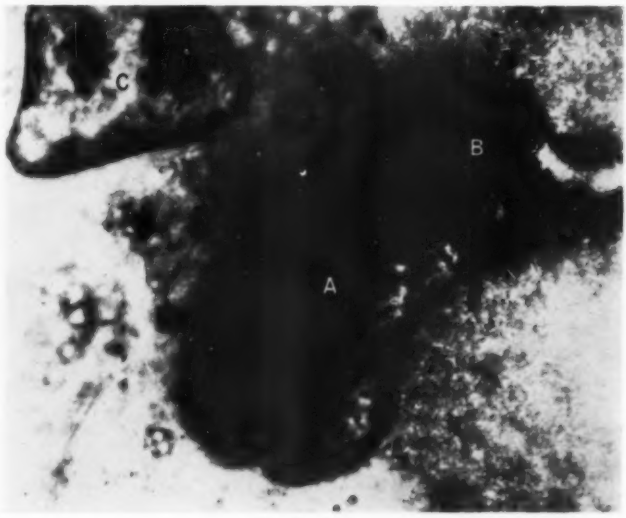

Fig. 6.—Three months after transplantation, inspection of chamber seems to indicate that fragments A and B are re-united, while fragment C definitely remains separated by connective tissue (200x).

FINDINGS

Rabbit I. Three pieces of stapes bone were placed in a chamber that had been established for two and one-half months as seen in Figure 5. Fragments A and B are closely approximated, while part C is slightly separated from A and B. The trauma to the chamber caused by this transplantation was followed by slight hemorrhage, moderate infiltration with leukocytes, and edema which all gradually subsided within ten days. New blood vessels began to connect the implants with the original chamber vessels within this time. The stimulus to vascular growth comes from the damaged foreign tissue and not primarily from injury to the host region.[15]

For the first few weeks of *in vivo* observation, the contents of the chamber displayed frequent changes, such as invasion by new blood vessels and considerable reshaping of the transplanted bones. Three months after transplantation (Fig. 6) the gap between particles A and B appeared closed. However, fragment C never came close to fragments A and B. Instead, a fairly large blood vessel had grown between them.

Four and a half months after transplantation, the animal developed unilateral hemiplegia and died of unknown causes. The chamber was opened, fixed with Heidenhaim-Susa solution, and its contents were removed for histological study.

Histological examination of these slides (Fig. 7) shows the final relationship between fragments A, B, and C. We see clearly that fragment C remained separated from fragments A and B, being surrounded by connective tissue which consists predominantly of collagenous fibers. By contrast, fragments A and B have grown together. They are also surrounded by connective tissue which encloses a layer of periosteum. The component parts of cartilage and bone and their typical cells are also visible.

Conclusion. The most important finding is that strand of fibrous tissue which connects the unified fragments A and B to the separate piece C. Hence, we see *both possibilities of fibrous and bony union in one specimen.*

Rabbit II. The chamber was installed on May 28, 1960, and three stapedial particles were transplanted on July 27, 1960. Two weeks later, Figure 8 was photographed on August 12, 1960. It shows a large number of newly grown blood vessels which connect the bone particles to the original chamber vessels. The largest fragment B showed beginning bone absorption in its central portion, undoubtedly resulting from insufficient blood supply to this area. To the right

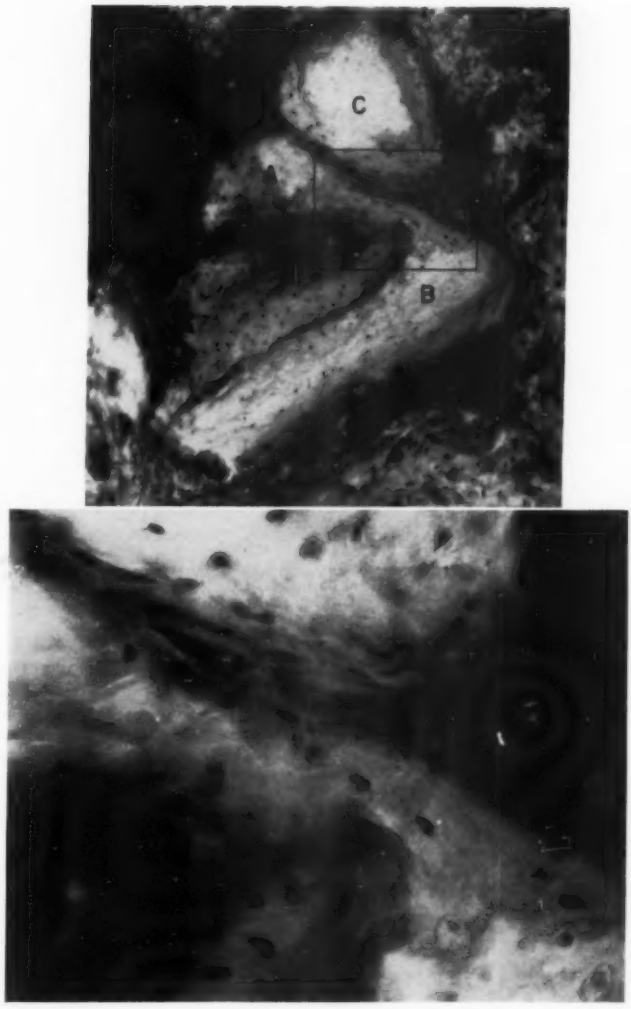

Fig. 7.—*Above*, histological slide of implants, showing osseous union of fragments A and B, and fibrous union between fragments A and C (500x). *Below*, enlarged view of area marked above, showing details of fibrous tissue strand, chondrocytes in center of fragment B, and osteocytes in fragment A (1200x).

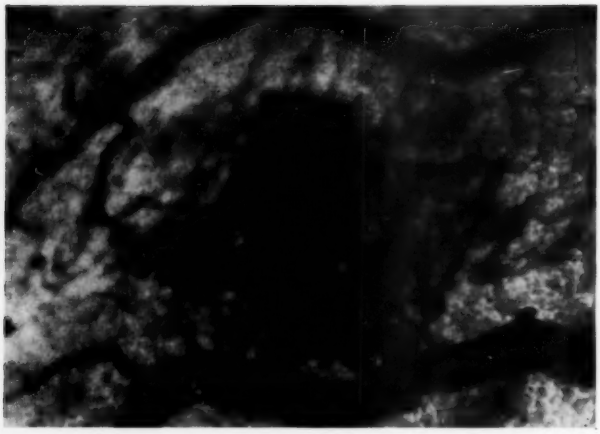

Fig. 8.—Pieces of fractured footplate two weeks after transplantation. Many blood vessels have grown from original chamber vessels towards implants (216x).

of the main fracture line lies fragment A. The smallest fragment C is on the left of fragment B. The fracture is indicated by the dark vertical line and appears under this magnification to consist of only one longitudinal split. In reality, however, it was a multiple fracture as seen in Figure 9 which was taken one month after transplantation.

Six weeks after transplantation, there was increased bony absorption in the center of fragment B and a smoother peripheral contour of all fragments, except on the upper edge of fragment A. Using higher magnification (250-500), one could still see the fracture lines and gaps between the fragments, especially between B and C. The accessory fractures between the lower portions of fragments A and B are revealed by dark heavy lines.

Eight weeks after transplantation, the sharp edged outline of fragment A had diminished as seen in Figure 10. At this stage, fibrous tissue began to surround the fragments. During the following weeks, osteoclastic and osteoblastic activity alternated at different sites on the periphery of and within the fragments. Three months after transplantation the sharp demarcation of the fracture line began to disappear. Moreover, the hole in the center of fragment B, described in Figures 8 and 9, had become smaller.

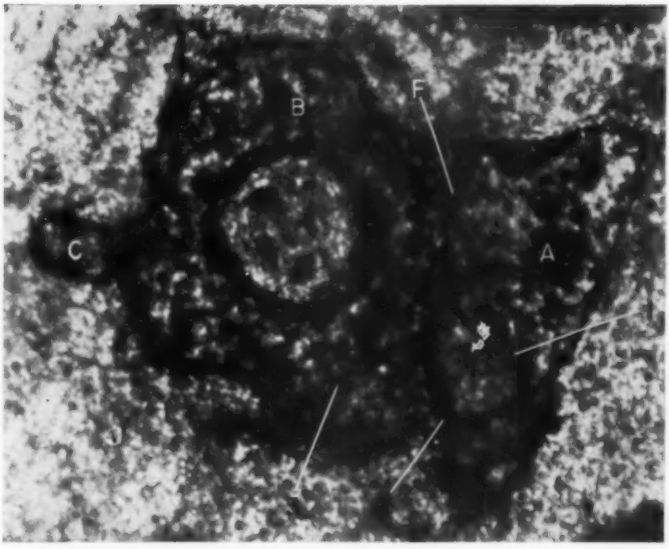

Fig. 9.—One month after transplantation. Note three fragments A, B, C; F = main fracture line; 1-3 accessory fractures. A large hole has formed in the center of fragment B (212x).

About four months after transplantation, we observe a single mass of bone instead of the previously described three separate fragments. This Figure 11 shows considerable new growth of bone from the area of fragment A. The fractures, indicated by dark lines in the previous histographs, have now completely disappeared. It follows that in this case all *fractures had healed by bony union* within about four months. Six months after transplantation we see in Figure 12 one completely rebuilt piece of bone without any signs of fracture. Its increase in size by a factor of about four is most impressive.

Since this animal will be kept alive as long as possible, future observations will be described in another paper. At that time, the final histologic findings will be compared with the chronologic behavior of the implants.

COMMENT

Although the technique needed for installation of the chamber and transplantation of tissue is rather simple, the control of the cham-

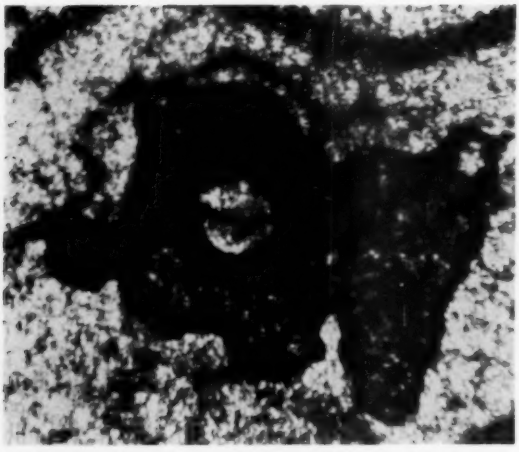

Fig. 10.—Eight weeks after transplantation. In contrast to the straight contours of the fresh implants (Fig. 8), their surfaces now appear more rounded. A blood vessel runs through the central hole of fragment B which has become smaller than in Figure 9. The fracture line is still visible. (147x)

ber's thickness, the photographing of its contents, and the strange appearance of the living specimen posed certain difficulties. In rabbit No. 1, for instance, *in vivo* observation of the chamber seemed to indicate that fragments A and B had become one single mass, while fragment C remained separated, but we could not be sure. Subsequent histological study definitely confirmed true bony union between fragments A and B, and fibrous union of fragments A and C by connective tissue. This uncertainty in interpretation of two different pictures of the same specimen obtained at different times and with two different techniques confused us at one point. Later we came to the conclusion that the difficulty originated from excessive thickness of the chamber contents. Albeit, the fact remains that this fracture had healed by both osseous and fibrous union.

We were also puzzled by the appearance of cartilage in the transplants. As stated by several authors,[2,3,8] considerable amounts of cartilage are contained in the footplate of the stapes where it articulates with the oval window. In our specimen (Fig. 7), a large area of cartilage was surrounded by bony tissue. From this observation we may assume that the fragments transplanted into our chamber were taken from the periphery of the footplate and not from its center as

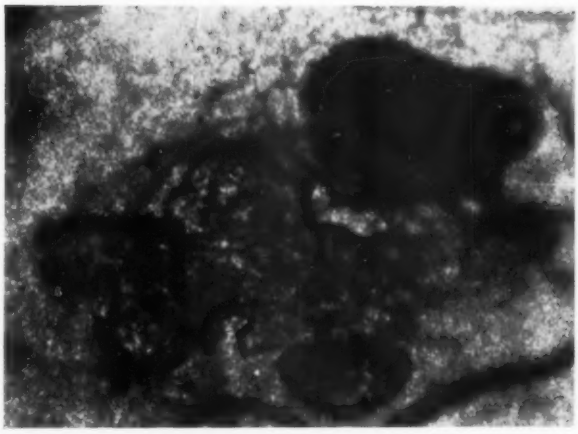

Fig. 11.—Four months after transplantation, a new outgrowth of bone is seen above the area of fragment A which appears blurred because it has undergone considerable absorption. The dark line between fragments B and C is a blood vessel. The main fracture line between A and B has disappeared (240x).

we had intended. This question appears important from the following viewpoint. Altmann and Basek[2] quote Oesterle by writing that "the footplate consists of two layers: an inner cartilagenous layer and an outer osseous layer. . . . This layer is usually thin, sometimes so thin that the footplate consists almost completely of cartilage." It is therefore not impossible that our transplanted fragments were actually derived from the stapedial center, as expected, and not necessarily from its periphery.

In rabbit No. 2, as well as in all further experiments, particular attention was paid to transplant the proper fragments with the greatest bone content. The thickness of the fragments and thus of the chamber were well controlled so that we were able to discern finer details of the consecutive tissue changes under the microscope. The detailed findings and the final outcome of these observations will be discussed in a subsequent paper.

As the illustrations show, multiple fractures of the stapes in rabbit No. 2 gradually disappeared within a period of four months. The regular growth of newly formed bone and the increasing obliteration of the fracture lines leave no doubt that this specimen has re-united

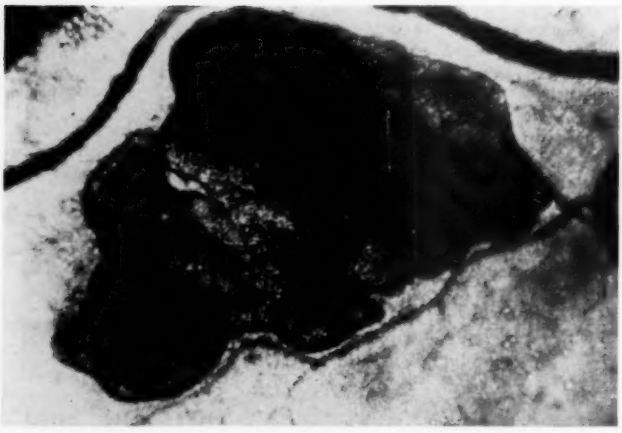

Fig. 12.—Six months after transplantation, the three original fragments have united to one completely rebuilt piece of bone which also has grown nearly four times bigger. Note its rich blood supply (140x).

by bony callus formation. As demonstrated with rabbit No. 1, these observations are evaluated best by comparing the in vivo and the final histological studies. After further study of tissues transplanted in this fashion it will be possible to describe and predict the outcome of these observations *in vivo* with considerable accuracy.

CONCLUSION

The tantalum chamber inserted into the rabbit ear lobe provides an excellent medium for implanted ear structures, such as parts of the stapedial footplate, because it contains healthy connective tissue and a very rich supply of blood. This environment serves as an excellent nutrient for the graft, for it closely duplicates its normal biological requirements.

There is no need for the constant supervision of culture media as is necessary for tissue cultures in vitro. This method has been found very convenient for the prolonged study of certain transplanted ear tissues because the specimens may be handled with minimal expense of effort and time, once the chamber has been properly installed and its subsequent micro-photographic observation has been organized. Little care is needed for the maintenance of the chamber; it will last

for several years, provided both the chamber and the animal remain healthy.

It would be premature to describe the generally valid behavior of stapedial fragments transplanted into the tantalum chamber. However, the two cases presented in this paper and the others under observation in our laboratory suggest that autogenous stapes (from the same organism) will survive, heal its fractures, and even grow, just as easily as the bones in other parts of the body. Future experiments will deal with the problems of isogenous (from the same litter), homogenous (from the same species), and heterogenous grafts (from another species).

While in rabbit No. 1 the fracture healed partly by fibrous union and partly by bony callus, rabbit No. 2 shows not only the bony healing of a stapedial fracture by callus formation, but also the formation of a rather large amount of new bone. After having observed a sufficiently large number of specimens, we shall be able to define the general trend in the healing of stapedial fractures in the particular rabbit race used for this experiment.

SUMMARY

The well established technique of *in vivo* tissue culture by means of the tantalum chamber inserted into the ear lobe of rabbits was employed for the study of tissue repair in fractured stapedial footplates. It could be shown that this method lends itself well for basic research in histopathologic problems of the ear.

As a preliminary report, two successful transplantations of stapedial footplate fragments are described. In the first case, the fractured segments healed by both fibrous and bony union as verified by subsequent histologic study. The second experiment showed bony union of the fractured pieces within about four months.

Since the chamber contents can be kept alive for the animal's remaining life span, the final histologic report on this second and similar experiments still in progress will be presented at some future date. These findings may become important for the theory and further development of stapedial surgery.

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Acknowledgement—Gratitude is expressed to Harry P. Schenck, M.D., Professor Emeritus of Otolaryngology at the University of Pennsylvania, for his help with this project; to R. G. Williams, M.D., Professor of Anatomy at the University

of Pennsylvania, for repeated consultations and teaching the technique to one of us; to Margaret Cubberly, B.S., for histologic and photographic assistance; and to Mr. John Goeller for all photographic work.

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LIV

PRIMARY ADENOCARCINOMA OF THE MIDDLE EAR

REPORT OF THREE CASES

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AND

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According to Schall[1] and others, the frequency of all types of neoplasms of the ear is between 1 to 5000 and 1 to 20,000 examined pathological ear cases. In 1951 Mattick and Mattick[2] reported that of all cancers arising from external, middle and inner ear only 1.5 per cent originate primarily from the middle ear itself. Gritti[3] found that among 25,539 cases of pathological ears only in one instance was it an adenocarcinoma. Primary adenocarcinoma arising from the middle ear are therefore considered by some clinicians to be "curiosities of medicine."

The first report of a primary adenocarcinoma of the middle ear in the world literature was given by Treitel[4] in 1898, who reported one case diagnosed by biopsy, without, however, mentioning treatment. Lange,[5] in 1904, reported, as he then noted, "the first case of primary adenocarcinoma." He described in detail a tumor which had metastasized into lymph nodes of the neck and chest. The diagnosis was made by autopsy and no treatment had been given.

Furstenberg,[6] in 1924, reported what appears to be the first patient treated by radical mastoid surgery, followed by irradiation. The patient was reported as still living four years and six months after the initial treatment. One year later, Heschlin[7] reported that he had operated on a patient twice, but did not employ irradiation. This

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Submitted as a candidate's thesis for the Chicago Laryngological and Otological Society.

patient died nine months following the initial surgery. The tumor was described as a carcinoma "cylindrocellulare."

Malan[8] described a case of adenocarcinmoa in 1926. This patient's diagnosis was confirmed by biopsy. Treatment was not given because the patient was in heart failure and died of this cause 18 days later. Malan noted that the tumor arose primarily from the middle ear mucosa in the hypotympanum. Gritti,[3] in 1934, treated a patient with adenocarcinoma by radical mastoidectomy and irradiation. At the time of the published report, the patient was well one year following the initial treatment. The tumor was described as having arisen from middle ear mucosa in close proximity to the orifice of the eustachian tube. Schall in 1935 reported the management of a patient with a primary adenocarcinoma of the middle ear by radical mastoidectomy and irradiation. This patient was living and well four years and two months following the initial treatment.

In 1940, Rosenwasser[9] treated a patient with adenocarcinoma of the middle ear by external radiation only. This patient died in a matter of four months. The tumor in this instance was reported as being extensively invasive. Grabscheid,[10] in 1943, was more fortunate with his patient who was treated by radical mastoidectomy and irradiation and was still living four years after the initial treatment. In 1954, Bradley and Maxwell[11] stated that the primary adenocarcinoma of the middle ear originates from mucous glands of the tympanum and that this type tumor is very rare and seldom metastasizes.

The present discussion is concerned with the report of three cases of adenocarcinoma of the middle ear, one of which, namely a primary papillary cystadenocarcinoma of the middle ear, we were fortunate to have pictorally well documented during a two year and three months continuous observation period, and also to have complete findings of postmortem examination.

REPORT OF CASES

CASE 1. A 45 year old white female, L.H., was first observed on March 31, 1954 in the department of otolaryngology of the University of Illinois, Research and Educational Hospital. At this time she stated that she had experienced vertigo about 12 years ago for approximately ten days. No diagnosis was made at that time. However, seven years later, following a severe upper respiratory infection, she noticed a full feeling in her left ear, combined with hearing loss and high pitched tinnitus, which has persisted ever since. In 1953, while being

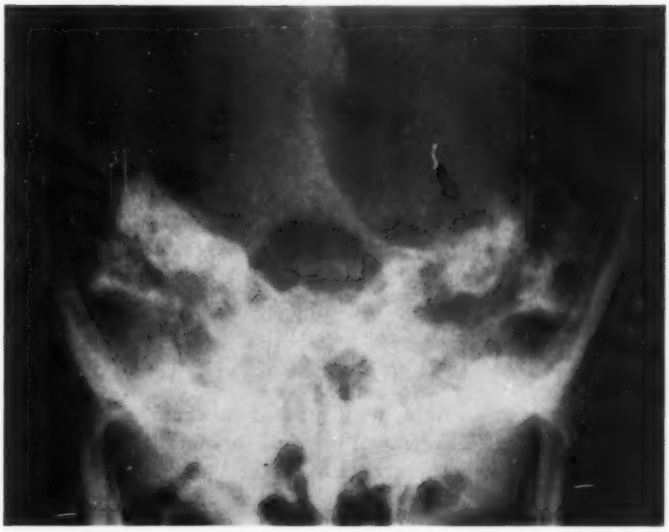

Fig. 1.—Showing an area of lesser density medial and lateral to the left arcuate eminence.

treated for a lymphedema of her left leg at Mayo Clinic, a discoloration behind the left ear drum was noted and was thought to be a chemodectoma. The patient declined further investigation at that time. Discharge from left ear began ten days prior to admission to our service.

Otological examination when first observed, revealed a whitish, readily bleeding mass, protruding through the posterior two-thirds of the left tympanic membrane, associated with a fetid discharge. There was no pain. The remainder of the nose, pharyngeal and nasopharyngeal examination was normal. Functional tests of hearing evidenced normal air and bone conduction on the right, but a severe conduction loss on the left, the affected ear. Bone conduction on the left was reduced to an average of 35 db. Vestibular function tests produced normal responses. X-ray studies of the mastoids revealed areas of lesser density medial and lateral of the left arcuate eminence (Fig. 1). Biopsy of the mass presenting itself in the left external canal was followed by brisk bleeding. Histologically, it was reported to be a papilliferous cystadenoma of the external ear canal, probably

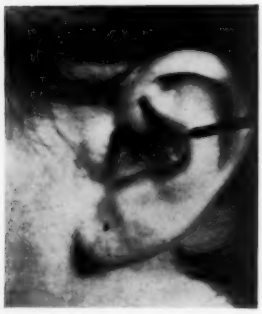

Fig. 2.—Mass filling the external auditory canal.

of ceruminous gland origin, with marked subacute inflammation of the adjacent tissue. The general physical examination did not reveal anything abnormal, with exception of the lymphedema of her left leg. No evidence of metastatic origin of the ear lesion could be established.

On May 6, 1954 the mastiod was entered and brisk bleeding tumor tissue was encountered which destroyed the medial portion of the posterior external canal wall, involved most of the middle ear and antrum, and eroded the dural sinus plate. Tumor tissue was removed extensively but it was impossible to do so completely in performing a radical mastoidectomy. Histological examination of the tumor revealed what was thought to be a papillary cystadenoma. Postoperative management was very difficult because of profuse bleeding each time the packs were disturbed.

From July 6 to August 26, 1954, surgery was followed by a total dose of 5500 roentgen units of standard external radiation. While towards the end of the radiation treatment the bleeding tendency abated, a fresh tumor began to fill the operative cavity, increasing slowly in size. In November 1954 the patient complained of a spasm of the left side of the face. This apparently had been going on for about the preceding six weeks. At this time the tissue filling the operative cavity was practically epithelialized. Electrical testing of the facial nerve activity (electromyography) evidenced a reduced response on the left side. In April 1955, x-ray studies of both mastoids did not evidence further changes in comparison with those taken soon after surgery. In August 1955, the patient again noticed slight

Fig. 3.—Tumor mass involving the entire left petrous bone.

twitching of the left side of the face. The mass had greatly increased in size and was filling the external ear canal (Fig. 2). In January 1956, the patient noticed double vision intermittently. It was at this time that a left abducens paralysis was evident. In February 1956 she began to have difficulty in swallowing solids.

A review, by the tumor conference, decided on no further intervention. At this time she fell into an excavation in downtown Chicago, when a sidewalk at a building site caved in, and had to be admitted to St. Luke's Hospital for a few days of treatment to an injured arm. In July 1956, the patient developed a numbness of the tongue and left side of her face together with facial weakness. The mass had increased in size. A left-sided beginning facial paralysis was noted, with inability to close the left eyelid and flattening of the nasolabial fold on the same side. In addition pooling of secretions in

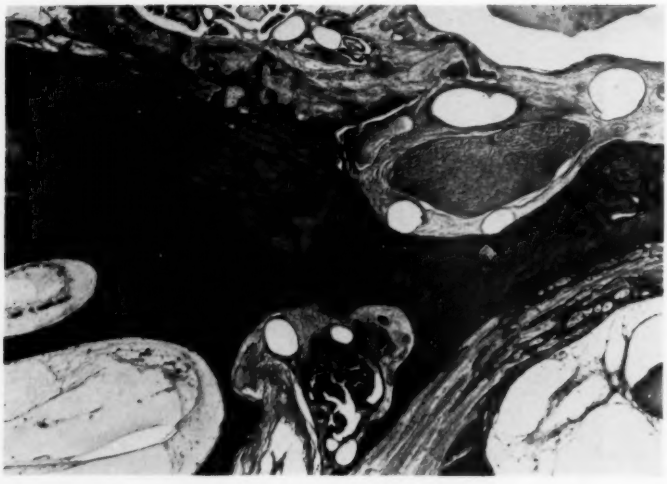

Fig. 4.—Tumor in the facial nerve canal medial to the geniculate ganglion close to the ampulla of the superior and horizontal canal.

the left piriform sinus and a left vocal cord paralysis were all noted at this time. These findings indicated the presence of a left sided jugular foramen syndrome. X-ray studies revealed findings compatible with progressive tumor enlargement. In August 1956, transient vertigo developed and in September 1956 patient was admitted for terminal care to the Illinois Eye and Ear Infirmary. X-ray studies at this time disclosed progression of bone rarefaction extending from the area of the mastoid defect into the petrous apex. During the ensuing few months the patient rapidly went downhill and expired in a state of coma in December 1956, two years and three months from the day when she was first observed by us.

The postmortem examination revealed the following:

Cranial Cavity: on opening the tentorium on the left, a multilobular, soft greyish-red mass was seen extending from the posterior surface of the petrous bone in the anterior surface of the left hemisphere of the cerebellum and into the brain stem in the region of the pons and just inferior to this level. Several of the cranial nerves were compressed on this side. The tumor measured 3.5 x 4.1 cm. The tumor was cut between the petrous bone and the brain stem, the latter

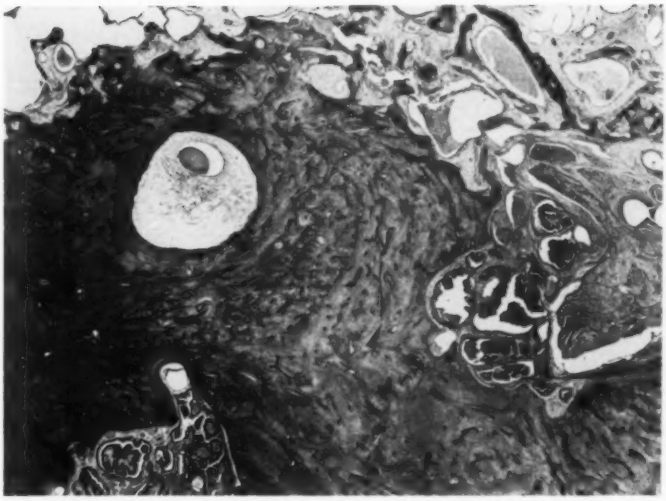

Fig. 5.—Geniculate ganglion invaded by tumor through facial canal from middle ear.

being fixed to the brain. The left temporal bone was virtually replaced and moderately enlarged by the presence of a similar soft, greyish-red tumor mass within it (Fig. 3). The right temporal bone appeared normal, as did the pituitary gland. The sella turcica was not involved or depressed by the tumor itself. The sphenoidal and ethmoidal sinuses were essentially normal.

Head and Neck: cervical lymph nodes, parotid and submaxillary glands were not affected. The oral cavity and nasopharynx revealed no abnormality.

Microscopic examination of both temporal bones, horizontally sectioned and stained with hematoxylin-eosin. The right temporal bone revealed no important abnormalities. The left temporal bone, however, evidenced the tumor tissue to be invading or replacing almost all mastoid cells and also the remaining portion of the middle ear. The stapes was found to be subluxated anteriorly and a portion of the anterior crus was observed to be interrupted and surrounded by tumor mass. Neoplastic tissue was seen to be invading the area between facial nerve and the horizontal semicircular canal, extending

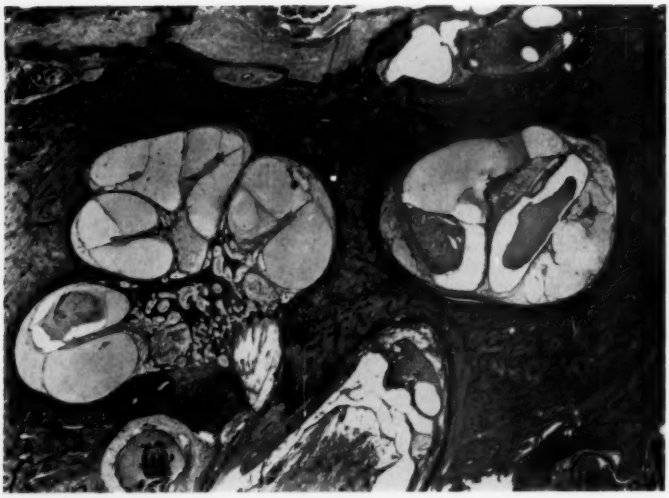

Fig. 6.—Tumor invading the internal auditory canal, causing atrophy of vestibular ganglion and spiral ganglion. Cochlea and ampullary portions of superior and horizontal canals reveal serofibrinous labyrinthitis. The crus of the superior canal contains tumor mass.

deeply into the Fallopian canal between the facial nerve and the ampulla of the superior semicircular canal (Fig. 4). The geniculate ganglion was also invaded by tumor (Fig. 5). The bony labyrinthine capsule was found to be eroded and partially destroyed. All three semicircular canals were partially invaded by tumor and marked infiltration was observed throughout the internal auditory meatus, beginning posteriorly. This invasion apparently ultimately led to atrophy of Scarpa's ganglion, the spiral ganglion, and to a serofibrinous labyrinthitis (Fig. 6). The semilunar ganglion was also infiltrated by neoplastic tissue (Fig. 7). The eustachian tube cartilage, as well as the carotid artery, apparently resisted the onslaught of the neoplasm, while the lumen of the tube was observed to be filled with tumor mass as far medially as could be followed in the sections (Fig. 8). The tensor tympani muscle was destroyed along with the semicanal housing it. Practically all bony tissue except some portions of the labyrinthine capsule had been destroyed.

The tumor tissue itself is comprised of a fibrous stroma with many blood vessels and a lining consisting of a double layer of cells.

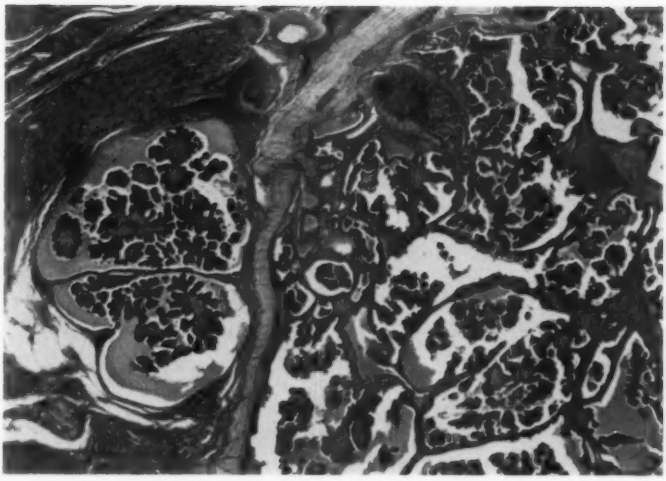

Fig. 7.—Tumor infiltrating the semilunar ganglion.

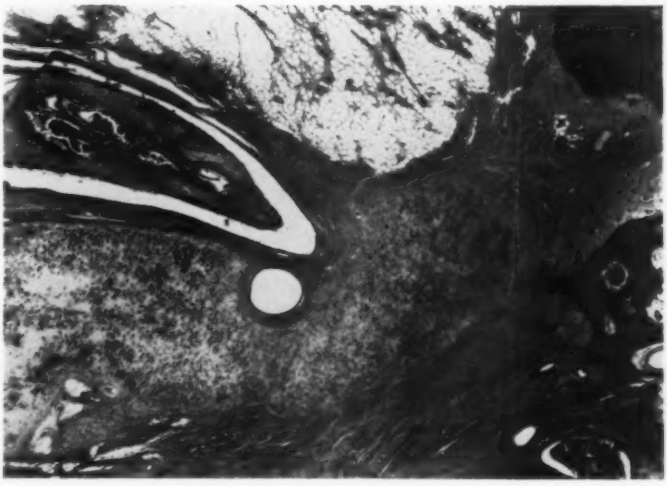

Fig. 8.—Tumor extending into the most medial portion of the eustachian tube.

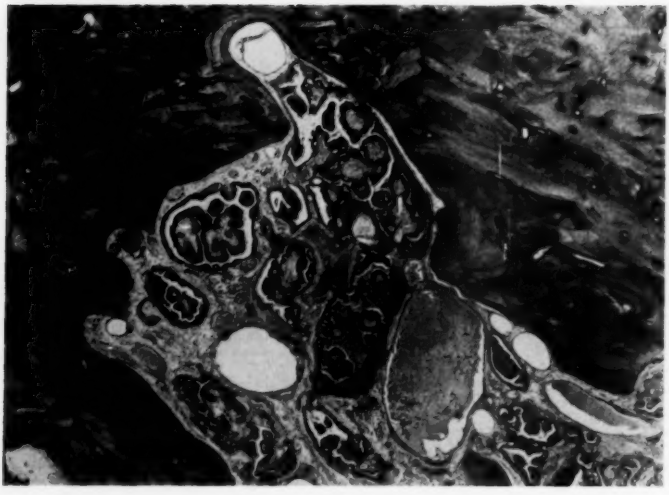

Fig. 9.—Showing malignant features of papillary cystadenocarcinoma of Case 1.

The cells of the outer layer present, in their basal third, a round, dark staining nucleus and pinkish staining protoplasm, while the remaining portion is filled with mucus. The inner layer of cells is composed of spindle-shaped cells which stain dark blue. These are recognized as myo-epithelial or "reserve" cells. Reserve cells bear the connotation that they have a potentiality to develop either into epithelial or muscle cells. In addition, multiple cysts containing mucus are observed. These are probably retention cysts formed by the mucus cells of the outer cell layer. In some areas quite a number of mitotic figures are observed; there is also pleomorphism and other malignant criteria present (Figs. 9 and 10). The cells forming the two layers lining the tumor stroma seem to arise from mucous epithelium, mucous glands, or their ducts. Since the tumor seemed to have arisen behind an intact ear drum and never presented itself in the nasopharynx, there remain but three sites from which it could have originated: the eustachian tube, the middle ear mucosa proper, or from the mucous membrane lining of the mastoid air cells. This neoplasm represents a papillary cystadenocarcinoma. While in some areas definite signs of low-grade malignant changes are present, it is locally aggressive and invasive. Clinically this tumor is characterized by a very slow growth, since the first symptoms of this patient were apparently noted in 1940.

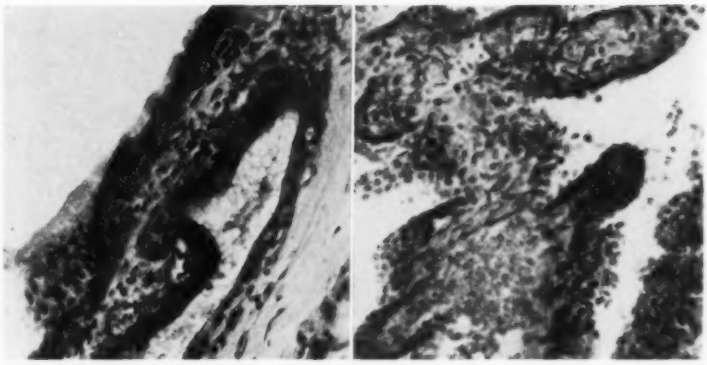

Fig. 10.—Early malignant changes of Case 1 in higher power.

It is suggested that this patient might have been saved by treatment if she would not have refused help at an earlier stage of her disease. This is, of course, conjectural.

CASE 2. A 30 year old white male, J.S., was first observed on June 27, 1958 in the department of otolaryngology of the University of Illinois, Research and Educational Hospital. The patient complained of hearing loss and drainage from the right ear of one year's duration. Therapy had included parenteral administration of penicillin and several myringotomies. Otological examination revealed a hyperemic right ear drum with a "nipple" like granulation in the inferior-posterior quadrant, and slight discharge. The findings in the remainder of the nose and throat examination were normal. Functional tests of hearing revealed normal air and bone conduction on the left ear but an average air conduction loss on the right of about 20 db. The bone conduction on the right was normal. Vestibular function tests revealed normal responses. X-ray studies of the mastoids demonstrated sclerotic changes in the air cell structures on the right. It was felt that the findings were compatible with subacute otitis media. The general physical examination did not reveal any abnormalities except for a right amaurosis due to a congenital cataract. The patient was treated with antibiotics, nasal decongestants, inflations and occasional myringotomies until, in October 1958, a granular polyp was noted at the marginal area of the upper posterior quadrant of the right tympanic membrane. These findings suggested either chronic otitis media with possible cholesteatoma or neoplasm of the middle

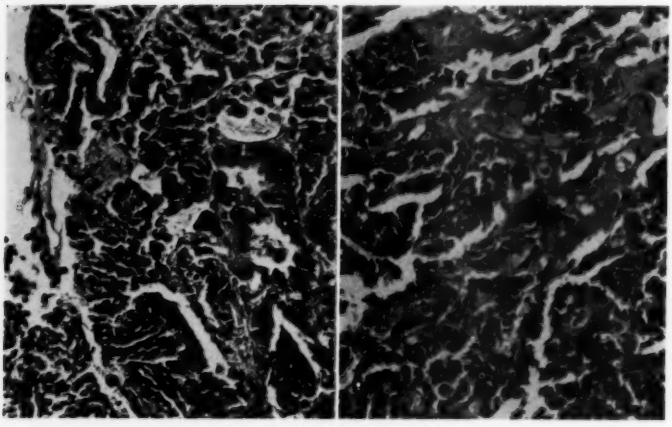

Fig. 11.—Malignant features of low grade adenocarcinoma. Left, Case 2; right, Case 3.

ear. Therefore, the mastoid was entered on January 13, 1959. The antrum and epitympanum were filled with what appeared to be granulation and fibrous tissue and the ossicles were intact and mobile. The lateral sinus was accidentally entered but the bleeding was controlled by applying gelfoam and gauze packs. Since the "granulation tissue" appeared neoplastic, more tissue was obtained from hypo- and mesotympanum as well as from the antrum and mastoid cavity. Examination of this tissue revealed a fibrous stroma containing epithelial cells. The latter cells were occasionally well differentiated and of the stratified ciliated columnar type. More often, however, the cells were poorly differentiated. These cells were occasionally columnar but mainly cuboidal in shape and contained rather uniform, dark, round or oval nuclei. There was a tendency to form acinar structures. In areas of more marked cellular pleomorphism no definite structural pattern was present. It was felt that this was a low-grade adenocarcinoma arising from the mucous lining of the middle ear, eustachian tube or mucous lining of the mastoid air cells (Fig. 11).

On March 3, 1959, an extensive radical mastoidectomy was performed. By sacrificing the tympanic membrane, incus and malleus and by partially displacing the facial nerve from its bed, it was possible to remove all pathological tissue from mastoid, antrum and the entire middle ear area. A right facial paralysis followed but completely

disppeared in three months. The operative cavity healed shortly thereafter. In November 1959 a small node was noted on the right side of the neck. Because the node became smaller and remained soft over a three months' period, it was felt that it did not represent a metastasis. The cavity has been re-examined at regular intervals to the time of this report without, however, evidence of recurrence of tumor.

CASE 3. A 35 year old white female, R.K., was first observed on July 9, 1958 by Dr. Robert Henner and one of us (C.J.). The patient complained of hearing loss and blocked feeling of the left ear of some duration. She also noticed slight bleeding while cleaning the external canal. Otological examination revealed a pinkish, firm polypoid mass with a smooth surface entirely obstructing the external auditory canal. The findings in the remainder of the nose and throat examination were normal. Hearing tests disclosed normal air and bone conduction on the right but an average conductive loss on the left of about 60 db. The bone conduction on the left side was normal. General physical examination, x-ray studies of the mastoids and vestibular function tests did not reveal any abnormalities. It was felt that the findings suggested either chronic otitis media, with possible cholesteatoma, or a neoplasm of the middle ear. Therefore, on July 17, 1958, at Michael Reese Hospital the left mastoid was entered by Dr. Henner and one of us (C.J.) and was found to be very cellular. The ear drum was largely destroyed and the polypoid mass found to arise from the posterior margin of the tympanic membrane, inferior to the *fossa incudis*. Ear drum remnants, the incus and the malleus were removed, and the middle ear, attic, and antrum were cleaned of all pathological tissue. A type III tympanoplasty was performed, using a free postauricular skin graft. Histological examination of the pathological tissue disclosed a fibrous stroma with numerous blood vessels and a lining consisting of a double layer of cells. Strands of this tissue were developing irregularly and occasionally formed structures which resembled acini. The cells of the outer layer were mainly cuboidal, but some of them were of the stratified ciliated columnar type. The cells of the inner layer were spindle-shaped and resembled "reserve cells." Marked cellular pleomorphism, without definite structural pattern, was predominant in most areas. The neoplasm was regarded as an adenocarcinoma arising from mucosal lining of the middle ear (Fig. 12). Therefore, on July 22, 1958, the mastoid cavity was re-opened, the packs removed and a total of ten radon seeds inserted, in the eustachian tube region, the hypotympanum, the stapes region, the attic and the mastoid antrum. One week later, a left sided facial weakness was noted. On August 18, 1958, the packs

were removed from the mastoid cavity. At this time complete facial paralysis was evident and the patient had severe vertigo, controllable only by Dramamine.® The patient returned to the hospital on November 3, 1958 and the sloughing skin graft and granulation tissue were removed from the cavity. Histological examination of the tissue evidenced only fibrous granulation with inflammation and necrosis. A biopsy from a granulating area of the cavity on November 25, 1959 failed to reveal neoplastic tissue which characterized the tumor mass. On May 5, 1960 a biopsy from a granulating area of the cavity disclosed only fibrous granulation tissue and x-ray studies of the mastoids demonstrated only the surgical and irradiation defects on the left side. Except for some difficulty in widely opening the mouth (present for several months), the patient is in good health at the time of this report.

CONCLUSION

The nine cases of primary adenocarcinoma of the middle ear reviewed in the literature and the three cases reported by us, originated from mucosa of the middle ear, eustachian tube or mastoid cells. Most of them are slow growing tumors of a low-grade malignant nature. Out of the nine cases of the first group only one was reported to have caused metastasis to other areas, in two others the tumor was only locally invasive. In our three cases metastasis were not observed and local invasion occurred in one instance only. This seems to favor the opinion of Bradley and Maxwell that tendency to metastasize is very rare in this type of neoplasm. The occurrence is apparently so rare that up to now not more than 12 patients have been reported in the entire world literature. Out of them six cases which had surgery and irradiation had the longest survival time, three of them lived four years and longer, one two years and nine months, one longer than one year and one is still living without evidence of recurrence two and a half years following treatment. Two patients had surgery only, one died after nine months and one is living and well one year and 11 months after treatment. In one instance with only radiation treatment, the patient died within four months. In three cases there was no treatment and these succumbed sooner. This seems to show clearly that these cases will respond best to combined treatment with adequate radical surgery and irradiation. The average survival time of four years or better is encouraging.

SUMMARY

Three cases of primary adenocarcinoma of the middle ear have been presented. There were nine similar cases reported in the world

literature, which were reviewed. The etiology, malignant nature, the tendency to metastasize and the frequency rate of this neoplasm have been discussed. By comparison, it was found that the treatment of choice is combined adequate radical surgery and radiation treatment which resulted in the encouraging survival time of four years or more.

1853 W. Polk Street

Acknowledgement—The authors express their sincere appreciation to Dr. Eleanor Humphreys and Dr. Francis Lederer for their invaluable help.

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LV

IMPACTED METALLIC FOREIGN BODY

(Reprinted, by permission, from the St. Louis Globe-Democrat of August 16, 1961)

The efforts of police, firemen and a surgeon were combined Tuesday afternoon to remove a bathtub faucet from the mouth of a five-year-old Alton boy.

M.E.C., son of Mrs. V.C., was placed in his bath about 4 p.m. A few minutes later, his mother saw him place his mouth around the tap-throat, and warned him not to do so, police said.

Mrs. C. said while her back was turned the boy lodged the faucet in his throat. She said the faucet was about six inches long, two-and-a-half inches in diameter, and was bent about two inches from the end.

When she was unable to disengage the boy from the faucet, Mrs. C. called police.

Police also failed to dislodge the tap, and called firemen. The firemen were unable to free the lad, so they hacksawed the faucet from the tub, and rushed him to St. Joseph's hospital with the faucet in the boy's mouth.

A hospital surgeon placed the boy under sedation and wrested the tap from his mouth without surgery.

Meanwhile, the mother was treated for shock.

The boy was reported in good condition Tuesday night, but remained at the hospital for observation. His mother was treated and released.

(Cf. Mosher "Life-saver."—Ed.)

LVI

BILATERAL CONTRACTION OF THE TYMPANIC MUSCLES IN MAN

EXAMINED BY MEASURING ACOUSTIC IMPEDANCE-CHANGE

AAGE R. MØLLER

STOCKHOLM, SWEDEN

The function of the intra-aural muscles has been the subject of many investigations. Most have been made on animals, such as rabbits and guinea pigs, where the contraction was elicited by a sound stimulus. The muscle contraction in these animals seems fairly well understood. In man, however, a detailed investigation has been more difficult to undertake than in animals. The acoustic impedance is almost the only parameter which it is possible to measure in normal living human subjects. Data obtained from experiments in man show that the results of animal experiments on these muscles cannot in detail be transferred to man. For instance, sound stimuli cause the contraction of both the stapedius and the tensor tympani muscles in the most commonly used experimental animals, in which the tensor reflex has a somewhat higher threshold than the stapedius muscle. This is not so in man, where the contraction of only the stapedius muscle seems to be elicited by a sound stimulus.

Most investigators assume that the contraction is bilateral in man as well as in the above-mentioned animals when only one ear is stimulated. It will be shown here that this is not the case in man. No real investigation on this problem has been undertaken before in normal living human subjects. Previous investigations of muscle contraction employing measurements of the acoustic impedance change have been made only for detection of the muscle contraction in the ear contralateral to that which is stimulated. A method of overcoming the difficulties in measuring acoustic impedance change at the stimulated ear will be described here.

From the Speech Transmission Laboratory, Division of Telegraphy-Telephony, Royal Institute of Technology, Stockholm, Sweden.

MEASURING THEORY AND APPARATUS

a. *Principles of Impedance Measurements.* The general principle for direct measurement of acoustic impedance involves measurement of the sound pressure at the plane of the unknown impedance when this is fed with sound through a high impedance. To get an output which is proportional to the unknown impedance, the sound pressure must be measured at this plane. The impedance which is then measured is, in fact, the unknown impedance in parallel with the impedance of the measuring probe and the sound source. If the change in the unknown impedance is small, the shunting impedance will affect the change in the total impedance only as a scale factor.

The impedance can also be determined by measuring the sound pressure at some plane nearer to the source. In that case the measured sound pressure will not be proportional to the unknown impedance.

b. *Apparatus.* A block schema of the apparatus used for measurement of the change in acoustic impedance of the ear is seen in Figure 1. It is a modification and extension of the set-up described earlier.[5] That apparatus was intended for indication of the change in impedance without any attention being paid to the proportionality of the recording to the impedance change. With the set-up to be described here, the recording is proportional to the change in impedance. The change in the acoustic impedance of both ears can be recorded simultaneously during the stimulation of one ear.

A tube is introduced into the auricular canal. To this tube two small hearing aid magnetic telephones are connected, one used as a microphone and one for stimulation. The sound (800 c/s) used for the impedance measurement is introduced through a narrow tube which is inserted in the larger tube (Fig. 1). A third magnetic hearing aid telephone is connected to the other end of that tube to provide the sound source. This telephone can also be used as a microphone for measuring the stimulation sound pressure at the end of the tube which is introduced into the auricular canal. The sound pressure used for impedance measurement is about 75 db re. 0.0002 μb or about 70 db above threshold of audibility.

The electrical output from the telephone which is used as a microphone is proportional to the sound pressure at the end of the narrow tube, which is in turn proportional to the acoustic impedance at this plane. This impedance consists of the impedance of the measuring device seen from the end of the tube together with the impedance seen from the end of the tube towards the ear drum. This last impedance

again consists of the air column between the ear drum and the tube together with the impedance in the plane of the ear drum. For relatively low frequencies, for which the wave length of sound is very large compared with the dimensions of the air column, this combination of impedances can be regarded as a simple parallel connection. A change of the impedance seen from the eardrum toward the middle ear will cause a change in the total impedance in the measuring plane. The measured impedance change is influenced by the shunting effect of the air column between the measuring tube and the ear drum and also by the impedance of the measuring device seen from the end of the measuring tube. The only effect of this influence will be to multiply the impedance change by a scale factor, as long as the impedance changes are small, and the frequency is low enough for the air column to be regarded only as a simple shunting impedance.

To measure the change in acoustic impedance caused by a muscle contraction, the electrical output from the microphone is balanced out by means of a voltage with adjustable phase and amplitude. This adjustment is made when no muscle contraction is present. When the acoustic impedance changes, the sound pressure will change and, consequently, the output from the microphone will change. Because the previous value is cancelled, the output will now be the difference in microphone voltage, which is proportional to the difference in acoustic impedance. It can be mentioned that the change in output from the microphone for a stapedius muscle contraction is only about 5 μV.

When the acoustic impedance is measured on that ear which is stimulated, the output from the microphone will contain both the stimulating frequency and the signal which is used for measuring the acoustic impedance. The sound pressure of the measuring signal must be kept so low that it will not influence the muscle contraction, which means that it must have a level well below the threshold for the muscle contraction. Therefore, the stimulating frequency will appear in the microphone output at a level which is very high compared with that of the signal used for measuring the acoutsic impedance. A great deal of the measuring signal is balanced out. Consequently, the signal-output is proportional to the impedance change, while the output of the stimulus frequency is related to the total impedance; in fact the ratio between the stimulating signal and the signal used for measuring the impedance change will be higher than the ratio between the stimulus sound pressure and the measuring sound pressure as measured at the ear. This makes the relationship between the measuring signal and the stimulus less favorable.

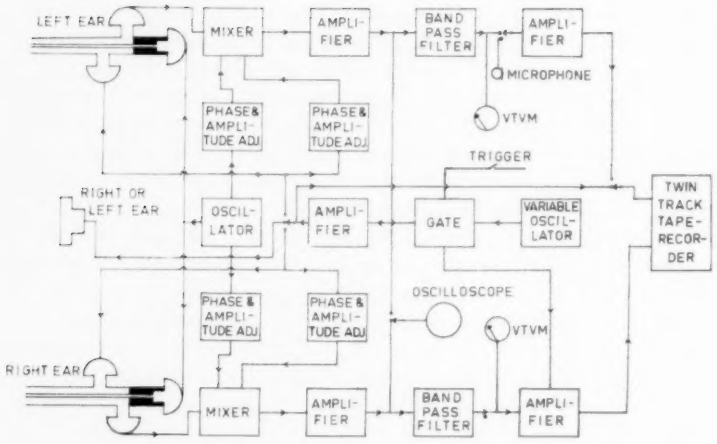

Fig. 1.—Block scheme of the apparatus used for measuring the impedance-change on both sides simultaneously.

The interference from the stimulus signal was so high that it turned out to be impossible to eliminate it only by filtering. If too sharp filters were used, the smoothing effect would be so great that it would be impossible to measure latency time or to get any idea of the real shape of the impedance change vs. time during stimulation. Because of this, another way was chosen. The stimulating frequency was balanced out in the same way as the signal used for measuring the impedance. Now the interference was decreased very much, but still a great deal of the stimulating signal appeared in the microphone output. Even if the stimulating frequency was canceled completely when the level was below the threshold of contraction, a great amount of stimulus would still appear in the microphone output when the muscle contracted. This was, of course, expected because at the stimulus frequency the ear impedance changes during muscle contraction. This change affects the balancing of the stimulus frequency. The degree of interference from the stimulus signal would be determind by the ratio between the level of the measuring signal and the level of the stimulus, provided that the impedance change and the microphone sensitivity are the same at both frequencies. This is not the case; and some advantage has been gained by choosing a value of measuring frequency for which the impedance change is greatest.

The filter which follows the amplifier (Fig. 1) is sufficient to remove the remaining energy at the stimulus frequency. The filter used here was a band-pass filter with a band width of 100 c/s and an attenuation of 36 db/oct.

It is also seen from Figure 1 how the output from both channels is recorded simultaneously on a twin-track tape-recorder. On one channel markings for the onset and the end of the stimulating tone bursts are superimposed, and on the other channel a microphone can be switched in for data recording.

c. *The Choice of Measuring Frequency.* The choice of frequency of the signal used for determining the acoustic impedance change is an important detail. Two phenomena should be taken into account when this frequency is chosen. The sound pressure in the ear must be well below the threshold of muscle contraction to avoid influence from the signal used in measuring the acoustic impedance change. This means that the frequency should be chosen in a region where the impedance change is great, and also bearing in mind that the threshold of muscle contraction is frequency dependent. The other phenomena are related to the inevitable changes in the connection between the measuring apparatus and the ear, including small impedance changes caused by blood pulsations. These changes can be assumed to be variations in the air volume between the measuring tube and the ear drum, which influence the measured acoustic impedance.

This means that the frequency should be chosen in a region where the ratio between the change in impedance and the total measured impedance is high. By looking at the data presented earlier,[6] it will be seen that this appears around 800 c/s where the change in impedance during muscle contraction is high at the same time as the impedance of the ear drum is low.

EXPERIMENTAL PROCEDURE

All the subjects used, whose ages were between 19 and 30 years, had normal hearing checked by continuous audiometry (von Békésy). They had never had any ear diseases or neurological diseases.

The subjects were sitting in a chair with the impedance-measuring devices connected to the ear in the same way as described earlier.[5] Sometimes the impedance change was recorded on both sides simultaneously, and sometimes it was measured on one side only, while the

other ear was stimulated with sound from a dynamic earphone (TDH 39). When the impedance was recorded simultaneously on both sides, the dynamic earphone was replaced by an impedance-measuring device similar to the one on the other side. The stimuli were sine-wave bursts of variable length. Normally a duration of 500 msec was selected and the shape was smoothed just enough to avoid clicks. The stimuli were presented at intervals of 5 sec or more with the intensity varied in steps of 2 db. The presentation was not rhythmic. The intensity was normally raised from a level below the contraction threshold and then increased in steps of 2 db until the maximum impedance change was obtained. Then the intensity was lowered again to a point below the threshold of contraction. When the impedance was measured on both sides simultaneously the same procedure was followed first on one side and then on the other side. A complete series of experiments was performed without removing the apparatus from the subject's head.

The balancing of the signal used for measuring the impedance was carefully watched by means of the VTVM's as shown in Figure 1. Changes in the balance were not always assumed to come from changes in the connection between the tube introduced into the auricular canal and the ear. In some subjects these changes were negligible, while for others it was necessary to readjust the balancing many times during the measurement. The changes did not seem to go in the same direction, but consisted of fluctuations around a constant value. Those persons who had great changes also often showed impedance changes for the blood pulsations to a higher degree those who did not display fluctuations in the impedance. The apparatus was held in a stable position by the head fixation, and the movements of the subject's head reinforced these changes very little. The subjects were instructed to swallow as often as they liked because swallowing would not cause permanent changes. Prohibition against swallowing could very easily cause difference in pressure in the middle ear cavity relative to the air pressure in the auricular canal. It was seen that very strong contractions sometimes, though not very often, caused small permanent changes in the impedance for some of the subjects. This could be expected because the muscle contraction caused a movement of the ossicles to such a great extent that small permanent changes in their position and small changes in the ligaments could very easily be caused.

The signals which represent the change in impedance were recorded on magnetic tape, as seen from the description of the apparatus. This made it possible to work up to one hour without interruptions.

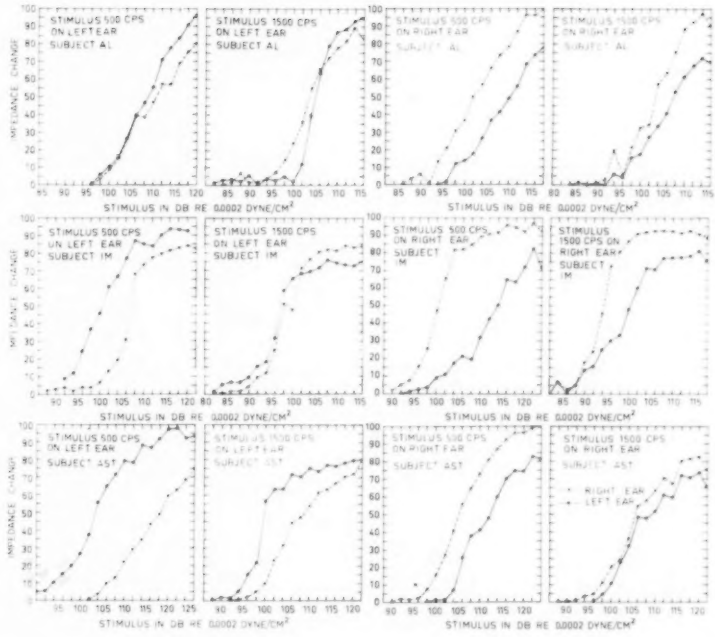

Fig. 2.—Change in acoustic impedance of both ears as a function of stimulus intensity for three subjects. The solid lines and circles show the impedance-change of the left ear, dashes and triangles show the impedance-change on right ear. The stimulus was changed in 2 db steps and raised from below threshold of contraction to a value where maximum impedance-change was obtained and then lowered again. Each point represents the mean of the values from the rising intensity and the falling intensity series.

The analysis can be performed at any convenient time following the test, and more than one recording can easily be made of the same data. Here the analysis was made by recording the intensity of the signals on a fast two-channel ink recorder or by means of a two-channel oscillograph.

MUSCLE CONTRACTION EXAMINED BY MEASURING ACOUSTIC IMPEDANCE CHANGE

Figure 2 shows the relation between stimulus intensity and change in acoustic impedance for both ears simultaneously.

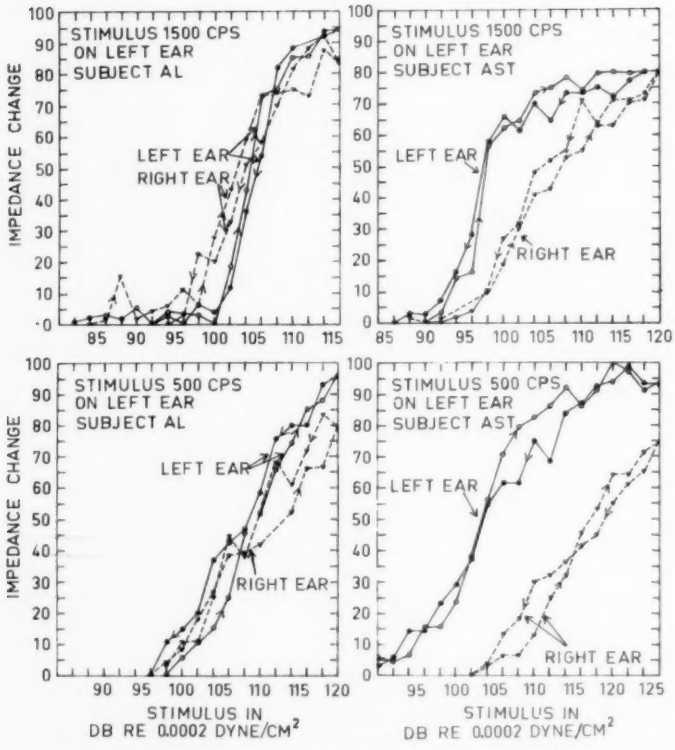

Fig. 3.—Impedance-change vs. stimulus intensity from an experiment where the stimulus intensity is raised from below threshold to a level which gives maximum impedance-change and lowered again to below the threshold.

The impedance change is measured at the time when the stimulus is switched off (duration of stimulus is 500 msec). To the left the left ear is stimulated, and to the right the right ear is stimulated. The impedance change is shown as a percentage of the maximum change. Maximum change is defined as the highest change in impedance during a complete experiment comprising the stimulation on both sides with two different frequencies (500 c/s and 1500 c/). The impedance change of the left ear is marked by circles connected by solid lines, and the impedance change of the right ear is shown by triangles connected by dashes. The values given in this figure are mean values of at least two measurements made directly after each other without

removing the apparatus from the subject's head. It is seen that individual differences are great, but all the subjects show results which demonstrate that the muscle contraction in man is not completely bilateral. In all subjects the ear which is contralateral to the stimulated ear exhibits a lower degree of impedance change than the ipsilateral ear.

It is normally seen that the curve of the impedance change of the ipsilateral ear versus stimulus intensity is somewhat steeper than is the case for the contralateral ear. At the same time it is seen for some of the subjects that the change in impedance reaches a level where overload occurs for a lower degree of impedance change on the contralateral ear than it does for the ipsilateral ear.

From Figure 2 it is seen that the curve of impedance *vs.* stimulus intensity has a steeper slope for 1500 c/s than for 500 c/s stimulus. These facts could be connected with the change in transmission through the middle ear.

It is also seen that the impedance change levels out near the threshold, which means that the threshold value is not a very precise determination. This is seen even more clearly from Figure 3 which shows the values of impedance change which occur when the stimulus is raised from below the threshold to a level which gives the maximum impedance change and lowered again to below the threshold. The results of two typical experiments are seen in Figure 3. In one of these the impedance change for a rising stimulus agrees very well with that for a lowering stimulus, while in the other there are great differences between the two measurements. This hysteresis could not be due to overstimulation because the last stimulation (when the level is lowered) gives a larger impedance change than the first, indicating higher reflex sensitivity.

In some subjects the impedance change has an unstable character over a stimulus intensity range of as much as 10 db during which the impedance change does not exceed 10 per cent of the maximum. In other subjects, however, the impedance change has a well defined threshold. This unstable contraction near the threshold coincides with the observations of Simmond,[7] who found that the threshold of muscle contraction in cats could be lowered by means of a short exposure of a moderately strong sound stimulus preceding the experimental stimulus. He recorded the action potentials in the muscles and reported a threshold shift of between 7 and 40 db at 1000 c/s.

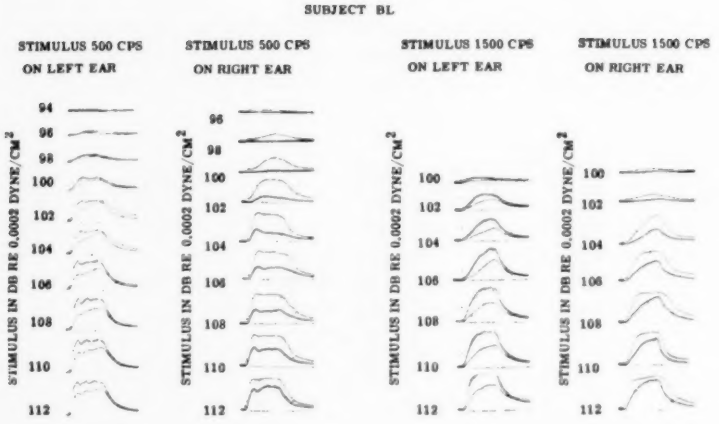

Fig. 4.—Impedance-change vs. time for different stimulus intensities for the contralateral and ipsilateral ear. Equal percentage of maximum impedance-change gives equal deflection. The curve showing the impedance-change of the right ear is interrupted 50 times per sec. The zero lines are indicated by dots. Stimulus duration is 500 msec and the onset of stimulus is shown by a spike in the recording of impedance-change.

The duration of the increased sensitivity was between 5 and 25 minutes.

Figure 4 shows the impedance change vs. time for different stimulus intensities. The deflexion is equal for both channels for the same percentage of the maximum impedance change. This was achieved by first measuring the amplitude of all responses and then finding the maximum value and correcting all the other responses to a percentage of that maximum value. After that the tape was analyzed again and the sensitivity on both channels adjusted to give the same deflexion for the same percentage of maximum impedance change. In Figure 4 the impedance change of the right ear is represented by dotted lines.

It is seen from Figure 4 that the shape of the impedance change vs. time curve is very similar in the ipsilateral and contralateral ear. From this figure it is also seen that the onset of the impedance change is much faster when the ear is stimulated with 500 c/s than when it is stimulated with 1500 c/s. Overshoot and very often a few waves of oscillation are seen in the beginning of the recording for a stimulus

frequency of 500 c/s. This is never seen for 1500 c/s and the observation reported here agrees well with what was reported earlier.[5]

THE COUPLING BETWEEN THE CENTRAL ACOUSTIC PATHWAYS

a. *The Central Acoustic Pathway.* The most important pathways from the ganglion of corti is rather well known[2] and most neurologic investigations of the ascending central auditory pathways show that the first and most important cross connection is maintained in the trapezoid body, which connects the right and left sides of the superior olive. The superior olive receives afferents from the cochlea nuclei. The lateral lemniscus is made up of fibers from the superior olive from both sides and the contralateral cochlea nuclei (dorsal and ventral). The lemniscus fibers end in the inferior colliculus which is connected to the acoustic cortex via the medial geniculate (Galambos, 1954; Stotler, 1953; Ades and Brockhart, 1950).

The reflex arc of the stapedius contraction, elicited by sound stimulus, proceeds out of the superior olive.[4] The pathway, which is put into action for an ipsilateral stapedius contraction, will then be: corti ganglion, cochlea nuclei (dorsal and ventral), superior olive and stapedius motor nerve. For the contralateral contraction the pathway is the following: corti ganglion, cochlea nuclei, superior olive, trapezoid body, opposite superior olive and opposite stapedius motor nerve. The term "opposite superior olive" is used for the side of the superior olive which receives its afferents direct from the cochlea contralateral to the stimulated ear.

b. *The Interaction Between the Two Central Acoustic Pathways.* Most investigations on the bilateral interaction concern the problem of localization. Many investigators used two clicks presented monaurally with some time difference and measured the electrical activity at different stages of the auditory pathway from the organ of Corti to the auditory cortex. Greatest response was found contralateral to the ear which received the first click. Others investigated the amplitude of the response of a single click presented monaurally. The amplitude at the side which is stimulated is always found to be higher than on the opposite side. This means that the response to an ipsilateral stimulation is smaller than that due to contralateral stimulation because of the crossing of the pathways. This type of investigation is more similar to the present study where the degree of muscle contraction is measured (recorded as degree of impedance-change) when one ear is stimulated by a sine wave. The degree of

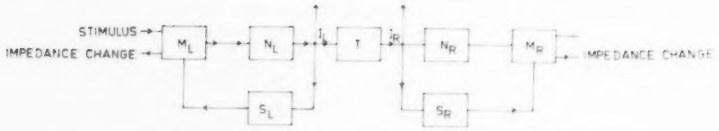

Fig. 5.—A simplified illustration of the bilateral acoustic pathways.

impedance-change is assumed to represent the activity in the superior olive.

Most investigations on the contraction of the intra-aural muscles elicited by a sound stimulus have been performed on the ear contralateral to the one stimulated. The majority of the investigators accept the contraction to be bilateral without giving any references to the case in point. Others[1,8] report that they could not find any difference in the reflex threshold when the ipsilateral or contralateral ear was stimulated. They did not mention in detail how the investigation had been performed. In a study of the function of the intra-aural muscles in normal unanesthetized cats, Galambos and Rupert[3] found that the latency of the muscle contraction on one side was almost independent of the side which was stimulated. These investigations were performed on cats in which a contraction of both stapedius and tensor tympani is elicited by a sound stimulus.

The conclusion of the foregoing discussion is that the neurologic investigations on the auditory pathways show clearly that the bilateral representation of monaural acoustic stimuli is not complete, but the contralateral ear is significantly more strongly represented than the ipsilateral ear. The investigations of the stapedius and tensor tympani contraction reported in the literature do not show any difference between ipsilateral and contralateral stimulation. The results reported here which were obtained from bilateral recording of the stapedius contraction in man elicited by sine wave sound stimuli, agree with the neurologic findings. The muscle reflex appears to be more sensitive to ipsilateral stimulation.

c. *The Bilateral Interaction Examined by Measuring Acoustic Impedance-Change Bilaterally During Muscle Contraction Elicited by Monaural Stimuli.* The degree of muscle contraction as represented by a certain percentage of maximum change in acoustic impedance in the auricular canal is assumed to be a measure of the nervous activity at the superior olive.

Figure 5 shows a simplified and presumptive scheme of the transmission from sound pressure input to change in acoustic impedance caused by a muscle contraction for left and right sides.

If the left side of Figure 5 is said to represent the left ear, and if the crossing of the nerve pathway is omitted, it is easy to see what will happen when, for instance, the left ear is stimulated and the impedance-change is recorded on both sides simultaneously. The pathways in that case are marked by arrows. A sound stimulus applied to the left ear passes block ML representing the middle ear and the block NL representing the pathway up to the superior olive where the activity is labeled IL. The signal can pass through the trapezoid body represented by block T to the superior olive at the right side. It is at this point where the signal which activates the right muscle branches out and the activity IR is represented by the impedance-change measured at the right ear. On the left side the muscle is stimulated by the signal which originates direct from the left superior olive (IL).

In this study the muscle contraction has been recorded by the change in acoustic impedance measured in the auricular canal. The acoustic impedance-change will then represent the activity at a level of the superior olive. The relation between this activity and the change of acoustic impedance is not simple but can be assumed to be similar for both ears and maybe even for different subjects. This makes it possible to use the change in acoustic impedance as a very easily obtainable measure for the activity at a point in the nerve system where it is impossible to get even the roughest estimate in normal human subjects.

In Figure 6 the difference in intensity required for the same degree of muscle contraction on the contralateral and the ipsilateral ear is shown. This difference is obtained from the plots of impedance-change as a function of stimulus intensity. In Figure 2 this difference is plotted as a function of the ipsilateral stimulus intensity. It is seen that the ipsilateral stimulation almost always requires smaller intensity to cause the same impedance change, which means that the sensitivity is higher to an ipsilateral stimulus. In most cases this difference is somewhat higher for a 500 c/s stimulus frequency than for a 1500 c/s stimulus. The difference between the ipsilateral and contralateral sensitivity increases somewhat when the stimulus level is raised. This is due to an earlier overstimulation of the contralateral ear, reducing the impedance-change in that ear.

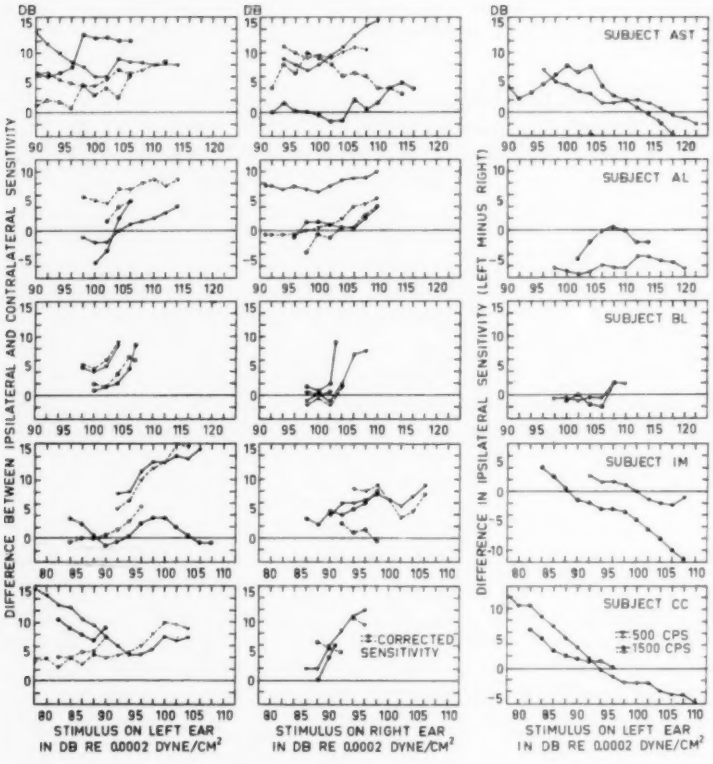

Fig. 6.—The difference in sensitivity of the ipsilateral and contralateral muscle reflex. Triangles are used for 500 c/s and circles for 1500 c/s.

On the right of Figure 6 is seen the difference between the intensity required for the same degree of ipsilateral impedance-change for the right and left ear. This difference in ipsilateral sensitivity is applied to the difference between contralateral and ipsilateral sensitivity to get a corrected difference (shown in Figure 6, by dashes, open circles, and triangles). It is seen that this corrected difference in some cases is somewhat less dependent on the stimulus intensity for relatively low stimulus intensities.

By examining Figure 5 it is seen that the difference between ipsilateral and contralateral sensitivity does not represent the attenua-

tion in the cross coupling which is assumed to appear at the trapezoid body (T in Figure 5), unless the sensitivity of the two ears is identical all the way from the entrance of the auricular canal to the superior olive. From the investigation of the difference in the sensitivity of the ipsilateral contraction (right side of Figure 6) it can be seen that a great difference is apparent and that the difference is dependent on the stimulus intensity. This difference represents the discrepancy in the transmission of the two ears from the auricular canal to the superior olive, including transformation of nervous activity at the superior olive to impedance-change. If the transformation of nervous activity to impedance change is assumed to be identical for the two ears, the measured difference in ipsilateral sensitivity will represent the discrepancy in transmissoin properties of the two ears from the ear drum to the superior olive. If the measured difference in sensitivity between ipsilateral and contralateral stimulation is corrected with regard to this, it will be a measure of the attenuation of the cross coupling between the two central pathways. This is valid provided that the transmission of the middle ear is not amplitude-dependent.

For ipsilateral contraction of the left ear the impedance-change is determined by:

$$\triangle Z_L = P_L \cdot M_L \cdot N_L \cdot S_L \cdot K_L;$$

where P_L is the sound pressure input at the ear drum. M_L and N_L is the transfer function of the middle ear, cochlea, and the primary auditory nuclei. $S_L \cdot K_L$ represents the relation between nervous activity at the superior olive (I_L) and impedance change (Fig. 5).

The ratio between sound pressure levels in the two ears for the same impedance change of the ipsilateral ear is:

$$\frac{P_R}{P_L} = \frac{M_L \cdot N_L \cdot S_L \cdot K_L}{M_R \cdot N_R \cdot S_R \cdot K_R};$$

When the left ear is stimulated the impedance change of the right ear can be expressed:

$$\triangle Z_R = P_L \cdot M_L \cdot N_L \cdot T \cdot S_R \cdot K_R;$$

The ratio between sound pressures in the two ears for the same impedance-change of one ear is:

$$\frac{P_R}{P_L} = \frac{M_L \cdot N_L \cdot T \cdot S_R \cdot K_R}{M_R \cdot N_R \cdot S_R \cdot K_R} = \frac{M_L \cdot N_L \cdot T}{M_R \cdot N_R};$$

If P_R is corrected according to the measured differences in ipsilateral sensitivity

$$\frac{P_R'}{P_L} = T ;$$

P_R' the corrected value of P_R.

It is seen that the impedance-change of the ipsilateral ear is dependent on the transmission properties in the ipsilateral middle ear, cochlea, central acoustic nuclei, and the reflex arc in addition to the relation between nervous activity and impedance-change measured in the auricular canal.

It is not known if the same change in volume velocity at the oval window at different frequencies gives the same change in activity in the superior olive and consequently, the same change in the impedance-change.

This activity can only be determined for stimuli with a level above the threshold of muscle contraction. At least for lower frequencies the muscle contraction will alter the transmission through the middle ear. This implies that the relation between sound pressure level and nervous activity is not the same during muscle contraction as below the threshold of contraction for frequencies where the transmission through the middle ear is affected by muscle contraction. As a rule the transmission is decreased during muscle contraction.

This implies that the activity in the superior olive will increase less for a certain rise in stimulus intensity above the threshold of muscle contraction than for levels below the threshold of muscle contraction.

The output from the middle ear will be

$$Pc = \frac{Pi \cdot M}{1 - \beta PiM}$$

where β is the transfer function of the amplitude regulating mechanism and M represents the transfer function of the middle ear without regulation. Pi is the level of the sound input to the middle ear.

A transmission alteration of the middle ear caused by the muscle contraction will make the measured difference in activity at the superior olive correspond to a greater change in sound pressure level at the ear drum than for levels below the threshold of muscle contraction. This also makes the measured difference in bilateral sensitivity too great, because the sound pressure at the oval window does not follow the sound pressure at the ear drum when this is varied. The change at the oval window is less. This could possibly be the reason why the observed difference in the level required for the same degree of muscle contraction on ipsilateral and contralateral stimulation was greater for 500 c/s than for 1500 c/s. 1500 c/s is supposed to be affected less by the muscle contraction than 500 c/s.

SUMMARY

A method is described for simultaneously recording the change in acoustic impedance in both ears when a muscle contraction is elicited by a sound stimulus applied to one ear. The measurement of acoustic impedance is performed by measuring the sound pressure when the ear is supplied with a constant volume velocity. When the change in impedance is measured, the impedance of the ear without muscle contraction is balanced out. Measurements of change in the acoustic impedance of the ear which is stimulated are complicated by the fact that the sound pressure level of the measuring signal has to be kept at a level well below the threshold of muscle contraction. The problem was solved by balancing out the stimulus signal which appears in the measuring circuit. Because of this the filter requirements are not very high and the impedance-change can be recorded with negligible distortion.

By recording the impedance-change simultaneously on both ears when one ear is stimulated, it is shown that a marked difference of 2-14 db in the sensitivity of the muscle reflex is apparent. The sensitivity is defined as the intensity required to give a certain percentage of the maximal impedance-change.

The central auditory pathways are discussed and the difference between ipsilateral and contralateral sensitivities of the muscle contraction is applied to a presumptive and simplified scheme illustrating the transmission from the ear drum to the superior olive and the transmission between the central pathways of the two ears.

The impedance-change caused by muscle contraction is assumed to be a representation of the activity in the superior olive. The possi-

bility of estimating the attenuation of the cross coupling from the difference in sensitivity of the muscle contraction due to ipsilateral and contralateral stimulation, is shown. The impedance-change shows overstimulation for a lower degree of impedance-change when the contralateral ear is stimulated than when the ipsilateral ear is stimulated.

ROYAL INSTITUTE OF TECHNOLOGY

The author is indebted to Dr. G. Fant for his generous support during this work. Thanks are also due to Mr. G. Rösler, who made the Békésy-audiometry on the subjects used in this investigation, and to those of my colleagues who participated in this investigation as subjects.

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The Scientific Papers of the American Otological Society

LVII

CIRCULATION OF THE INNER EAR FLUIDS

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Corti, in 1851,[1] described the cells of the stria vascularis and suggested that they might be the structure for secreting endolymph. Also in 1851 Reissner[2] described the membrane which now bears his name and divides the scala vestibuli from the scala media, showing anatomically that the membranous labyrinth is a closed system. Following this observation there has been much speculation concerning the characteristics of the endolymphatic and perilymphatic fluids. In 1927 Stacy Guild[3] performed an experiment which he felt furnished sufficient evidence to indicate the nature of fluid flow within the scala media.

Through a small pipette Guild injected a solution of potassium ferrocyanide and iron ammonium citrate into the scala media of several living guinea pigs. After the lapse of various time intervals, the animals were sacrificed and the acid in the fixation fluid precipitated prussian blue granules in sites along the scala media. The temporal bones of these animals were then sectioned and mounted serially so that the location of the granules could be studied with the microscope. In 16 of 20 animals the blue granules were found in the walls of the endolymphatic sac. From this he concluded that the flow of endolymph was from the stria vascularis down the scala media through the canalis reuniens to the saccule ending finally in the endolymphatic

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sac after passing through the endolymphatic duct. Since that time considerable knowledge has been gained concerning the chemical constituents of the two inner ear fluids.

By careful analysis Catherine Smith and co-workers[4] have shown that perilymph is very high in sodium but low in potassium whereas the endolymph is high in potassium and low in sodium. According to Guild's theory of the flow of endolymph, the monovalent ions of the endolymph would be derived from the blood supply within the stria vascularis. Somehow the high sodium and low potassium of the blood serum would be changed as the stria makes endolymph in which the reverse condition exists. This newly formed endolymph then is secreted into the scala media passing down the extent of the scala until reaching the saccule, endolymphatic duct and sac. Figure 1A indicates schematically this theory.

Since Guild's article there have been many different suggestions concerning the flow of the endolymph and the manner in which the cells of the organ of Corti are furnished with the nutritive materials. Recently Naftalin and Harrison[5] have proposed what we might call a radial flow theory as compared with the longitudinal flow theory of Guild. These authors suggest that the fluid flow proceeds from perilymph through Reissner's membrane to endolymph with the stria vascularis acting as a selective absorbing site. A function of Reissner's membrane is to prevent the flow of potassium from the scala media to the scala vestibuli. The stria vascularis by an ion exchange system analogous to that of the renal tubular cell extracts sodium and exchanges potassium for it. Potassium cannot pass Reissner's membrane except by relatively slow equimolecular exchange for sodium so that the amount of potassium builds up in the scala media until the required concentration is reached. The concentration of potassium in the endolymph is dependent upon the ratio of the volume of endolymph to the plasma flow through the stria vascularis per unit time, and equilibrium is determined by the structural characteristics of Reissner's membrane. More information is needed concerning the morphology of this important structure. This very interesting and intriguing theory is shown schematically in Figure 1B.

Much conflicting evidence has accumulated concerning these two types of theories. Guild mentions in the beginning of his article that he was attempting to use a method similar to that used previously

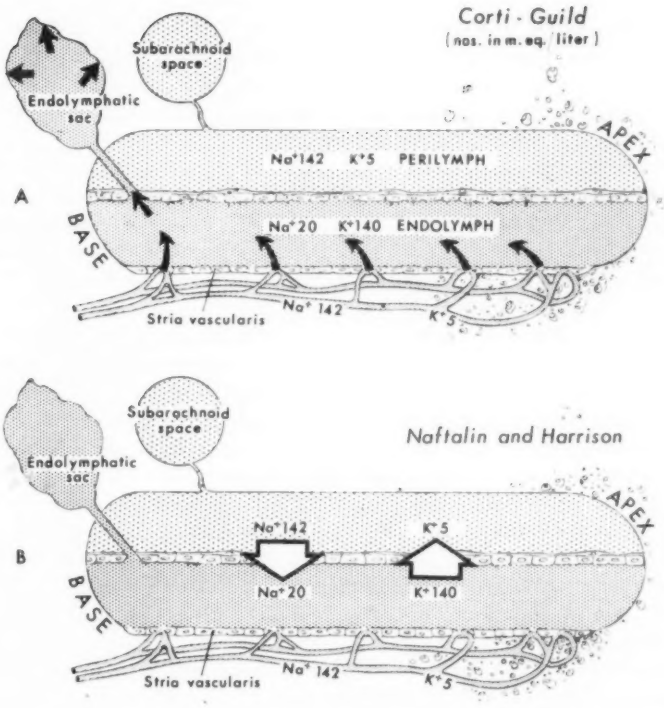

Fig. 1.—Two different theories of fluid circulation within the inner ear. (*A*). Corti suggested that the stria vascularis is the source of endolymph and Guild on the basis of his experimental results, suggested that there is a constant flow of endolymph from the stria past the organ of Corti to the basal end, eventually ending in the endolymphatic sac. (*B*). Naftalin and Harrison have suggested that endolymph is made from perilymph and that the stria vascularis is an absorbing structure. The numbers indicate the amount of electrolyte in blood serum, endolymph and perilymph.

for determining the direction of flow of cerebrospinal fluid. In a recent review of the "blood-brain barrier" system, however, Dobbing[6] has recommended that the use of such foreign material be discarded. He has come to this conclusion after a review of all of the relevant experimental evidence which seems to show that such procedures do not give valid results. These substances injected into the body tissues are not normal solutions and the reaction of the tissues may be different from what it would be under normal conditions. Another factor which raises doubts concerning the longitudinal-flow theory comes from the results of experiments in which attempts have been made to block the endolymphatic duct.[7] When such procedures are carried out there is no subsequent distension of the scala media as Guild suggested would result from the accumulation of endolymphatic fluid within the scala media.

On the other hand recent experiments tend to support the Naftalin-Harrison type of theory. Dolman, on the basis of radioisotope studies, believes that his experiments show endolymph to arise from the stria vascularis and to pass directly into the tectorial membrane. This is a radial flow opposite from the direction postulated by Naftalin and Harrison but is still a radial-flow theory.

In two recent papers[8,9] we have presented evidence which seems to provide added support to the radial-flow theory. It has been shown by Davis et al.[10] that injections of artificial perilymph into the scala media abolish, in the region of injection, the responses of the organ of Corti as manifested in the cochlear potentials. Békésy[11] has indicated that, as he looks through Reissner's membrane down onto the organ of Corti, should perilymph flow through a break in Reissner's membrane thus contaminating the endolymph of the scala media, the oil-like droplets which are the hair cells become opaque and the organ of Corti non-functional. On the basis of this evidence, and, if there were a longitudinal flow of endolymph, one would expect that a tear in Reissner's membrane would allow the perilymph to flow towards the base within the scala media killing the organ of Corti from the region of the Reissner's membrane tear all the way basalwards to the canalis reuniens. By means of a special stain[12] which stains endolymph darker than perilymph we have shown in one of the earlier papers[8] that a rupture in Reissner's membrane allowed perilymph to flow into scala media but that this perilymph did not destroy the organ of Corti all of the way to the basal end. This type of break in Reissner's mem-

brane was produced from within by the excessive vibration of the cochlear partition.

In another experiment reported recently[9] we showed that surgical injury to particular areas of the scala media did not result in complete deterioration of the organ of Corti either towards the apex or towards the base. In fact, the region of injury seems to remain confined to that particular spot unless excessive damage is done to the bone of the walls of the cochlea, in which case the entire system fills with bone. There are also indications from some of our earlier work[13] that, in the case of injury to Reissner's membrane, it can repair itself, thus re-establishing the continuity of the scala media.

In our paper on "Fluid Barriers Within the Otic Capsule" presented before the recent meeting of the Academy, an experiment using guinea pigs was reported briefly in which we recorded the cochlear potentials from the scala tympani of the second turn and the scala tympani of the first turn during and following a rupture in Reissner's membrane of the second turn brought about by the introduction of a small probe into the scala vestibuli of that turn. We reported that over a period of forty minutes there was a loss of response up to 14 db in the second turn while that in the first turn did not change at all. In later experiments we have continued this recording over a longer period of time. In this paper we report a continuation of this experiment.

There are two parts to the following report. The first is an electron microscope examination of the basilar and of Reissner's membranes and the second is a measure of the flow of the inner ear fluids determined by recording the cochlear potentials through time as a small injury in Reissner's membrane of the second turn in guinea pigs is produced.

ELECTRON MICROSCOPY OF THE BASILAR AND OF REISSNER'S MEMBRANES

From several guinea pigs the cochlea was removed and opened so that the membranes of the inner ear were exposed. This was immediately immersed in buffered osmic acid fixative. Following fixation the soft tissues were carefully dissected away from the bone and carried through processing for electron microscopy.

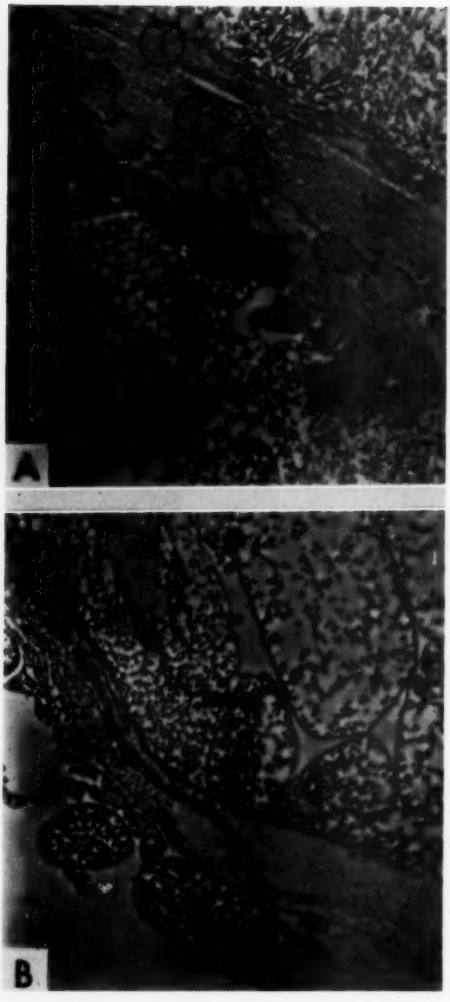

Fig. 2.—Electron micrographs of the basilar membrane of a guinea pig. (*A*). The four layers appear beneath Claudius cells (upper right). (*B*). Beneath the foot of the outer pillar cell the membrane splits to include layer No. 2. Layer No. 4 also originates at this point. Deiters cells and tympanic lamella border the membrane.

Figure 2A and B are electron micrographs of the basilar membrane. Other reports[14,15] have described electron microscopy of the basilar membrane but have not revealed in detail the four layers as shown in this figure. The cells in the upper right hand corner of Figure 2A are Claudius cells, the next layer is a continuous one which consists of radial fibers proceeding from the spiral osseous lamina all the way across to the spiral ligament and on up behind stria vascularis. Beneath this layer is the second one which consists of longitudinal fibers. This layer only extends from the external pillar cell to the point of attachment on the spiral ligament. The third layer is one which appears quite nodular and contains radial fibers. These also extend from the region of the external pillar cell out to the spiral ligament extending downward to its attachment on the wall of the scala tympani. The fourth layer also starts from the region of the external pillar cell and expires at its attachment to the spiral ligament. As can be seen this is quite an irregular layer of longitudinal fibers. It has many finger-like projections which extend down into the cells of the tympanic lamella appearing in the lower left hand corner of the figure. Figure 2B shows the outer pillar cell in the center and portrays how the main layer of the basilar membrane separates at that point into the two types of radial fibers and includes between them the two layers of longitudinal fibers. The cells in the lower left hand corner are those of the tympanic lamella.

Figure 3 is an artist's schematic conception of these layers of the basilar membrane. In the center is the organ of Corti indicating the total picture. In the upper right hand circle is a blown up portion of the external pillar cell showing the point where layers 1 and 3 separate to include the layers of longitudinal fibers in region 2. The longitudinal fibers of region 4 are shown between the radial layer of 3 and the tympanic lamella. The lower picture is a cutaway to show the nature of these different layers. It would appear from this type of structure that the basilar membrane exists strictly for the purpose of providing strength for the mechanical vibrations which are brought about by sound. It does not appear likely that the basilar membrane, with so many different layers all of which are fibrous, would have any properties of selective diffusion.

Reissner's membrane in this same guinea pig material was also examined. Figure 4 is an electron micrograph of a region from a guinea pig's Reissner's membrane. It is seen to be composed of two

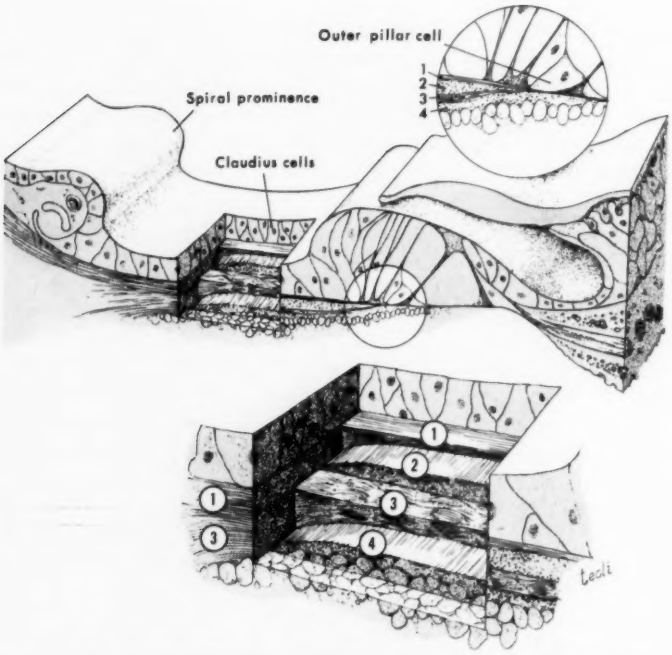

Fig. 3.—A schematic representation of the layers of the basilar membrane. The circled area in the upper right shows the region of the foot of the outer pillar cell where the uppermost layer of the basilar membrane splits into two to include the layer labeled No. 2 made up of longitudinal fibers. Layers No. 1 and 3 extend from the outer pillar cell to the spiral ligament where layer No. 1 extends up behind the stria vascularis and No. 4 extends downward within the spiral ligament. Layer No. 4 starts in the region of the footplate of the outer pillar cell and extends over to the point of attachment to the basilar membrane as does No. 3. Layers No. 2 and 4 consist of longitudinal fibers.

layers of cells. On the scala media side is a layer of cuboidal cells which are not very large but are closely packed and continuous. There are numerous microvilli extending down into the endolymph. On the perilymphatic surface are extensive squamous cells the membranes of which, after including the nucleus, come close together so that there is a very small amount of cytoplasm between them. These layers of

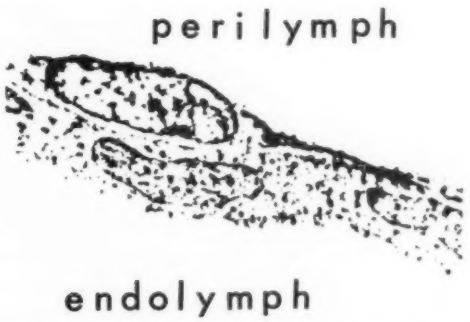

Fig. 4.—An electron micrograph of Reissner's membrane. The endolymphatic layer consists of a layer of uniform cuboidal cells with microvilli extending down into the scala media. On the perilymphatic side the cells include a large nucleus and very little cytoplasm. The membranes of these cells flatten down against each other and extend over a great distance along the membrane.

cell membranes on the perilymphatic side extend over large areas so that there may be only four nuclei between the point of attachment on the spiral limbus and that at the upper edge of the stria vascularis. Figure 5 is the artist's schematic conception of this membrane. The two layers of the membrane are clearly portrayed and the numerous microvilli extending from the cuboidal cells on the scala media side down into the endolymphatic fluid are clearly portrayed. These microvilli tremendously increase the surface area of the cells. Generally, the villi, as they exist in the subarachnoid spaces or the intestines, are there for the purpose of absorption, but those villi are relatively large and are composed of many individual cells. The microvilli on the cuboidal cell layer of Reissner's membrane are parts of the surface membrane of these individual cells, and lend some support to the Naftalin and Harrison notion that this membrane acts as a selectively diffusable one with cells of large surface area on the scala media side for the control of the potassium content within this space.

EXPERIMENTS ON THE FLOW OF ENDOLYMPH

Method. In the following experiments the function of the organ of Corti was determined by measuring the electrical activity of the

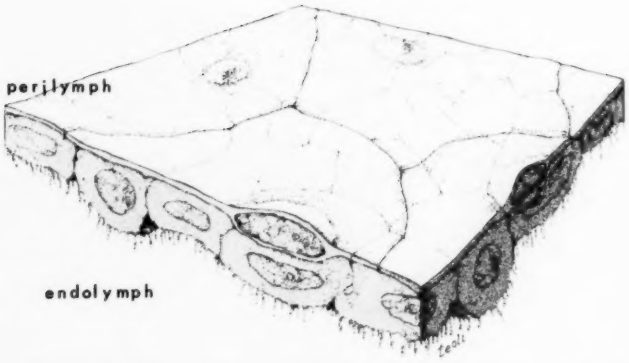

Fig. 5.—A schematic representation of Reissner's membrane showing the cuboidal cell layer with microvilli on the endolymph side and large flattened squamous cells on the perilymph side.

sensory cells accompanying the introduction of sound. The methods of stimulation and recording have been described in many previous papers. The important part of this procedure concerns the location of electrodes. In order to minimize the number of holes and the possible loss of fluid from the cochlea, single electrodes were used in the basal turn (ST_1), the second turn (ST_2) and the third turn (SV_3). The response recorded at each of these three electrodes was amplified by a Tektronix Type 122 amplifier. The outputs of these amplifiers went to a switch so that any one of the three could be selected at choice. The switch led to a General Radio Type 736A wave analyzer. The 50 kc signal within the wave analyzer which corresponds to the magnitude of the input signal was tapped and led to a logarithmic converter and then to the Y axis of an X-Y recorder. The X axis reflected changes in the amplitude of the stimulating tone. Control of this amplitude was by means of a motor-driven sweep-attenuator which made possible increases or decreases in intensity from that level which gave the lowest level of response to a level which overloaded the ear of the animal. By this means intensity functions could be plotted for any number of frequencies from any of the three turns in a matter of seconds. This was done not only to save time during the experiment but to prevent producing damage to the organ of Corti by maintaining stimulating tones too long.

Two methods of recording were actually used. One was a continuous recording in which a low-level tone was maintained in the ear while the output was recorded. Thus, the decrease in response which might follow the invasion of the scala media by perilymph could be plotted with time. The other method of recording consisted of periodically running intensity functions by means of the sweep amplitude stimulator and the X-Y recorder.

Insertion of the electrodes into the cochlea demanded special precautions. It was, of course, desirous that no structures of the organ of Corti be damaged in any way by the surgical procedure. By a specially constructed hand drill, small holes, about 90 microns in diameter, were drilled first in the scala tympani of the first turn. A stainless steel electrode about 190 microns long was then inserted into the hole. A small epoxy bead fit into the holes snugly at the 190 micron mark so as to prevent further entrance of the electrode and minimize the escape of fluid. Fluid was further prevented from escaping by sealing the electrode in position with a pre-warmed agar-gelatin mixture. The same procedure was carried out in the other two turns. At the termination of the experiment the electrodes were removed and the entire middle ear filled with the agar-gelatin mixture so as to prevent the further escape of fluid. The animals were then perfused intravitally and sent through histology. All of these ears have not yet come through histology but there have been enough now studied under the microscope to show that the penetration of these electrodes was as planned.

Once these three electrodes were placed and normal intensity functions taken another small hole was drilled in the scala vestibuli of turn two as nearly directly above the electrode of ST_2 as possible. Into this small hole, which was about 120 microns in diameter, a small hook was inserted and carefully turned so as to do no further damage than breaking Reissner's membrane. This procedure did not always work perfectly. On a few occasions the stria vascularis was injured as would be evidenced by the appearance of a small amount of blood. Also, without extreme care, rather extensive injury to the organ of Corti would be produced as evidenced by a rapid drop in the responses of electrode in ST_2. However, when this latter occurred it did not change the experiment to any great extent because, if perilymph were to flow toward the base, it would not make any difference whether the organ of Corti in the second turn were damaged or not

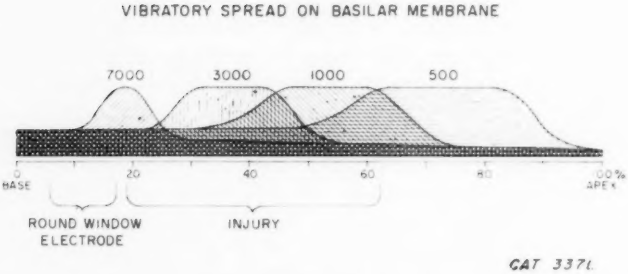

Fig. 6.—A schematic representation of the vibratory spread of selected frequencies along the basilar membrane. These data represent the accumulated results from many different experiments on overstimulation. Also indicated is the region of injury produced in a cat by a probe inserted into the basal turn. This was purely a mechanical injury with no contamination of the scala media by perilymphatic fluids. A bracket indicates the position, in this animal, of the round window upon which was placed a silver foil electrode. This injury resulted in intensity functions, recorded at the round window, as indicated in Figure 7.

except that there would be a slight initial drop in the ST_1 response brought about by loss of response contributed by those cells of ST_2.

Results. There are several factors which have to be taken into account in this experiment, and these make interpretation rather difficult. In the first place, we have to consider the distribution of the vibratory pattern along the basilar membrane for the different frequencies. Low tones, of course, will activate the apical end of the basilar membrane and high tones the basal end, so that the selection of frequency is important in determining the direction of flow of perilymph once it enters the scala media.

There is also to be considered the placement of the rupture in Reissner's membrane. As we have stated, this was in the region of the electrode placement in ST_2 and it becomes necessary to interpret the region of damage with respect to the frequency distribution along the basilar membrane.

A third factor which has to be considered is the placement of the electrodes. It is well established[16] that there is an attenuation of the electrical response arising from any particular part of the scala media

as these electrical responses proceeds from that point to an electrode position. This means, in other words, that an electrode records greater responses from those sensory cells to which it is the nearest. We must then carefully consider the frequency chosen with respect to the electrode position.

Before we could start our experiments on the effects of rupturing Reissner's membrane we needed to know just how responses to different frequencies would be altered with respect to an electrode in a particular position if the organ of Corti were injured in a certain spot.

Two cats were used in this series of experiments. A platinum-foil electrode was placed on the round window membrane and a small probe introduced through a hole in the scala tympani of the first turn away from the round window so as to approach the basilar membrane from the scala tympani side and produce damage to the organ of Corti without breaking Reissner's membrane. These animals were later perfused and studied histologically so that the region of injury might be plotted.

Figure 6 is a schematic representation of this experiment. The basilar membrane is shown stretched out in a straight line and upon it are plotted what we now know to be the general area of distribution of the various frequencies. This evidence is obtained from a large number of different experiments on stimulation deafness where injury to the regions of the basilar membrane have been produced by excessive sound at particular frequencies.[17] It is shown in this figure that the peak of the 7 kcps (kilocycles per second) frequency is around 19% of the distance along the basilar membrane from the basal end. The center of action for 3 kcps appears at about the 38% point, its maximum extending from 25% to about 43%. One kcps centers around the 48% point with its maximum extending from 43 to 62%, and 500 cps extends over a wider range with its center around 68% extending from the 62% to the 85% region. The round window of this particular cat extends from the 8% to about the 18% point. The platinum-foil electrode was resting in the center of the round window so it is assumed that the potentials were picked up from the region over which the round window extends.

The small probe which was inserted through the hole in ST_1 in this particular cat dislodged the spiral ligament in such a way that

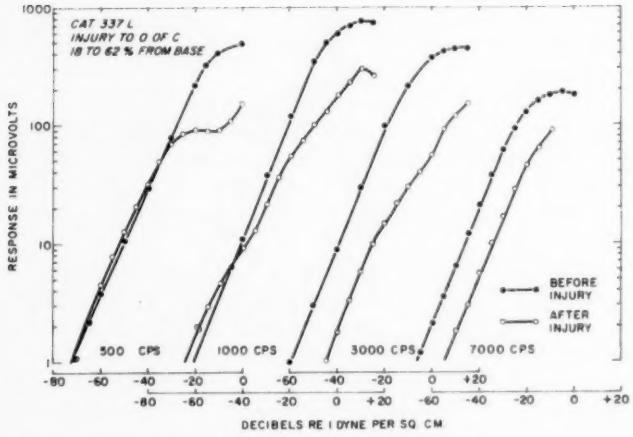

Fig. 7.—Intensity functions following the injury shown in Figure 6 as recorded from a platinum foil electrode on the round window membrane. An injury to the region of maximum vibration shifts both the intensity and the dynamic range of the response, whereas an injury to a region of the organ of Corti removed from the area of maximum vibration does not alter sensitivity but alters the dynamic range, decreasing the ear's response to the more intense tones.

the organ of Corti was pushed into the scala media dislodging it from the basilar membrane but not breaking Reissner's membrane nor the basilar membrane. This was a fortunate type of injury because this now produced damage to the organ of Corti of a mechanical nature without the entrance of perilymph. Microscopic examination showed the extent of this injury to be greater than had been expected. The injury extends from the 18% to the 62% point from the basal end. By keeping in mind the distribution of frequencies along the basilar membrane, the extent of injury, and the site of the electrode, the effect upon the function of the organ of Corti as revealed in its electrical response can be predicted. The region of maximum activity for 500 cps is little affected by the injury so one would expect little change in the magnitude of response although, as indicated, there is considerable spread of activity towards the basal end. The maximum response area for 1 kcps and 3 kcps falls within the region of injury; 3 kcps more so than 1 kcps. One would expect 3 kcps to be more

seriously affected. Seven kcps is partially affected by the region of injury and is also close to the electrode. Since the response area for 7 kcps is not spread out as much as that of the lower frequencies one might expect that the region of injury would more seriously affect the response than a similar injury to the lower frequencies.

Figure 7 shows the intensity functions for these various frequencies. The intensity of the tone relative to 1 dyne/sq cm is shown on the abscissa and the electrical response from the ear of the animal is shown along the ordinate. An important fact is revealed by these intensity functions. There are two kinds of changes that take place: shifts in the sensitivity of the ear at low levels of stimulation and in the overloading of the ear at high levels of intensity. We note that at 500 cps the sensitivity at low levels has not shifted but that the ear is no longer able to respond at as high a sound intensity level as before. Referring again to Figure 6 this is easy to understand in view of the well established principle that as intensity of a tone increases the response pattern spreads along the basilar membrane. At low levels the region of injury to this animal's ear has no effect at all upon the region of maximum activity, but as sound intensity increases, the spread of action moves more and more towards the base and into the region of injury. Here the organ of Corti is not able to respond in the normal fashion so the response loses its dynamic range for this frequency. Practically the same thing is true for 1 kcps.

Although histologic studies showed that the injury extended into the region of maximum response for 1,000 cps, the electrical response seems to indicate that, at low levels of stimulation, there were a sufficient number of healthy hair cells to give a normal response, but that as sound intensity level was increased, the spread of response moved more into the injured region so that the ear was not able to respond with the same magnitude as normally. No doubt, because the region of injury extends further into the 1 kcps area than it does into the 500 cps area, the early departure from linearity of the injury curve is explained.

The region of maximum activity at 3 kcps is wiped out by the injury and so as the intensity functions show there is a loss in sensitivity as well as an early departure from linearity. The intensity functions for 7 kcps show a loss in sensitivity and an overloading at a lower response level. Perhaps the injury extended a little farther

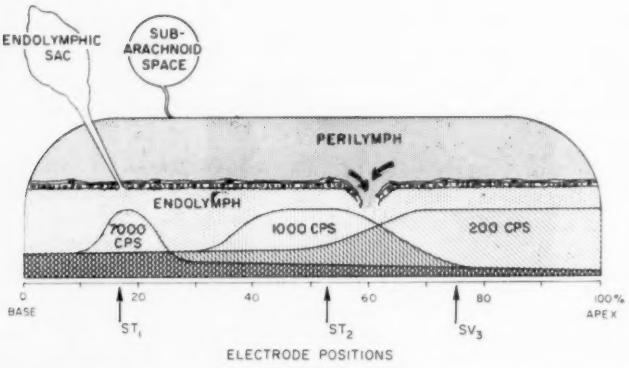

Fig. 8.—A schematic representation of the experiment performed to determine the flow of inner ear fluids. The three electrode positions and the vibratory spread of various frequencies are represented along the basilar membrane in terms of percent of position from the basal end. Reissner's membrane was broken by means of a small hook introduced into the scala vestibuli in the region of the second turn just above the point of insertion of the second turn electrode. These electrodes were inserted and sealed in ST_1 and ST_2 and SV_3.

into the base than the schematic diagram from the histologic plot shows.

We have now at hand, then, two factors that must be taken into consideration when studying the effects of the spread of toxic perilymph throughout the endolymphatic system. If perilymph were to affect the sensory cells at a point removed from the center of maximum activity for a particular frequency, the first sign of injury one would expect to see in the electrical recording would be an earlier departure from linearity, with a maintenance of low-level sensitivity. As the toxic effect of perilymph slowly spreads to the regions of maximum activity we would observe a loss in sensitivity.

In Figure 8 there is a schematic representation of this particular experiment. The positions of vibratory spread along the basilar membrane are taken from the same data as the plot in Figure 6. The location of the rupture to Reissner's membrane and the location of the electrodes varies somewhat from animal to animal. Also it is necessary to keep in mind that the electrodes do not record from an area strictly isolated within the region indicated by the arrow but

record from a broad area, with responses from sensory cells greatly removed from this site being attenuated more than those close to the electrode. The site of rupture of Reissner's membrane is approximated by judging the position of the injury with respect to the round window in the basal end of the cochlea. The histology of these animals is not complete so the exact interpretation of the positions of electrodes and Reissner's membrane injury are not yet known. This, however, is not important in the interpretation of these results.

If the type of injury, as shown in Figure 8, actually were produced then we might expect the following results. For the electrode in the ST_1 position and for 200 cps, we might expect a slight shift in sensitivity immediately upon entrance of perilymph into the endolymphatic system because the perilymph would spread somewhat to the region of maximum activity of the frequency, but we might more readily expect to find an early bend over in the function since, as intensity is increased the response would move into the region of damage. Results can also be predicted for the ST_1 electrode for injury to the 1 kcps response. Since 1 kcps is on the electrode side of the injury, very little change in sensitivity, but an early bend over in the intensity function, would be expected. As time progresses, considering a longitudinal flow of endolymph, the perilymph should gradually move down into the region of maximum activity for the 1 kcps region and one would expect dramatic changes in sensitivity. Somewhat the same results would be expected from 7 kcps recorded at ST_1. This frequency and electrode position should be the most sensitive indicator of the flow of the fluids through the scala media. As perilymph continues to flow into the scala media from the tear in Reissner's membrane it should eventually reach the 7 kcps point and reduce its sensitivity considerably. Stacy Guild reported that, in an animal that had been sacrificed 45 minutes after the injection of the potassium ferrocyanide, granules were noted in the ductus reuniens on the basal end of the scala media. If the rate of flow is rapid then one would expect the 7 kcps response to be affected within this length of time. One would, of course, expect the greatest amount of shift in sensitivity to occur from both the electrode in ST_2 and that placed in SV_3.

A total of 20 guinea pigs was used to check the above predictions.

Figure 9 shows typical results from these experiments. After rupturing Reissner's membrane recording was continued for 3 hours

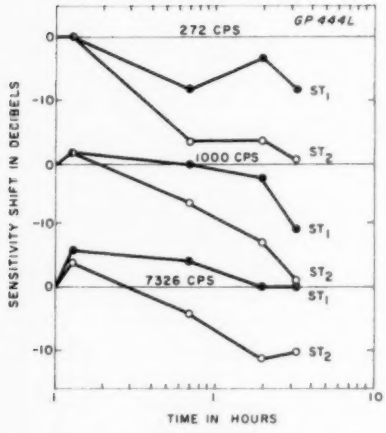

Fig. 9.—The results on a typical animal, of an experiment as shown in Figure 8. If perilymph, pouring through the tear in Reissner's membrane, were swept towards the base by a flow of endolymph as indicated by Guild's study, then the toxic effects of the perilymph should be manifest on the recording of the 7 kcps region within 45 minutes as Guild indicated. Here very little effect is shown for a period of three hours and 15 minutes. The electrode in ST_2 indicates a more severe progressive damage.

and 15 minutes. The results show that for the ST_1 electrode over this period of time there has been no loss in sensitivity for 7,326 cps. (The odd frequencies shown in these charts were used because of tube resonances in the stimulating system. The particular frequencies shown were at a resonant point for the tube and gave the most acoustic output for the particular settings of the stimulating equipment.) The ST_2 electrode shows a slight improvement 15 minutes after injury which proceeds to drop gradually, but at the end of two hours stabilizes and even shows a beginning recovery. For 1 kcps the ST_1 electrode shows no change over a period of approximately two hours and then shows a sudden drop, whereas the ST_2 electrode, after an initial improvement at the 15 minute point, shows a constant decrease. The response to 272 cps at the ST_1 electrode shows a drop of about 8 db at the end of 45 minutes but tends to remain constant at this level up to a period of 3 hours and 15 minutes. ST_2 electrode shows

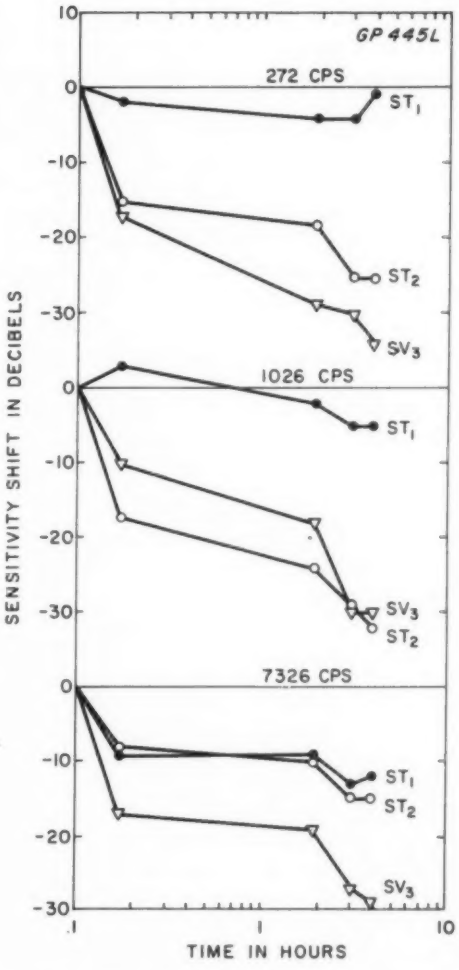

Fig. 10.—The results from another animal similar to that of Figure 9. The curves show the electrical response of the cochlea as recorded from the indicated electrode positions following a tear in Reissner's membrane in the second turn.

a rapid drop during the first hour which then tends to stabilized up to 3 hours and 15 minutes.

Figure 10 shows a similar experiment on another animal which, in addition, had an electrode in SV_3. Observing the responses to the ST_1 electrode it is seen that there is very little change over a period of three hours for 272 cps and 1026 cps. In this case 7326 cps shows an initial drop of about 10 db which then levels off and seems to parallel that of the injury of ST_2 electrode. The rupture to Reissner's membrane must have been a little more towards the base in this animal than that shown in the schematic diagram of Figure 8. The noteworthy observation is that the response does not proceed to drop progressively over time as one would expect if injurious effects of the invading perilymph continued. There is also evidence that the injury to Reissner's membrane may have been rather extensive because of the type of responses seen from the electrode in the third turn. This progressive loss of response is not easy to explain for this electrode position. One would not expect the perilymph to be carried into the apical turns by fluid flow. Perhaps Reissner's membrane is torn over a greater area.

If the direction of endolymph flow is towards the base, as Guild has stated, and, if, within 45 minutes, fluid from the upper turns should reach the basal turn and even endolymphatic sac, one would expect deleterious effects of perilymph to show up within three hours to an electrode recording at the basal turn. Neither of these animals show this to any great extent. There is an initial change which shortly stabilizes and tends to remain constant. Even on the second turn electrode there seems to be a stabilization after three hours.

It was observed earlier that one of the first manifestations of an injury, remote from a region of maximum vibration to a particular frequency, is an early overload of the ear. This is accounted for by the fact that injury to cells remote to the region of maximum amplitude means no response from this remote region with spread of activity as intensity is increased. Less voltage is produced at these levels of stimulation than under normal conditions.

Figure 11 shows the curves that were made on the X-Y recorder from the same guinea pig whose sensitivity response is represented in Figure 10. The electrode in ST_1 shows some shift in sensitivity which is reflected in the curves of Figure 10, but also it shows an increasingly

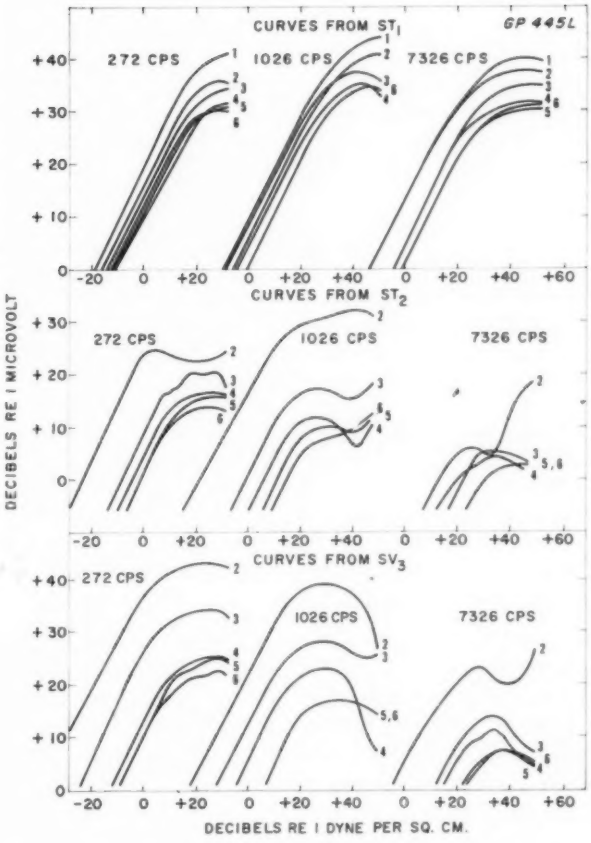

Fig. 11.—Intensity functions taken periodically during a four hour period for the animal whose changes in sensitivity are shown in Figure 10. As would be predicted from a radial- rather than a longitudinal-flow theory the electrode in the first turn shows very little change over a period of time. The numbers at the ends of the curves indicate the length of time elapsed. Curves labeled 1 were those taken before any holes other than the electrode hole in ST_1 were drilled. Curve No. 2 represents the intensity functions taken immediately prior to the rupture of Reissner's membrane with all three electrodes in place and the holes sealed. Curves 3 were taken after a time lapse of 3-15 minutes following injury. Curves 4 represent 105-126 minutes after injury, curves 5 represent 170-185 minutes after injury and curves 6 represent 215-225 minutes post injury. No curve 5 for 1026 cps from ST_1 was taken.

more marked bend over at the high response levels. The numbers on the curves are the same as the points plotted in Figure 10. Curve 1 of ST_1 was a standard curve taken before any other hole except that in ST_1 was drilled. Curve 2 is a measure taken immediately before injury. It is quite noticeable that after the lapse of approximately two hours the curves tend to be quite similar and even on occasion show an improvement. These are indicated by curves 4, 5 and 6 on the chart.

The curves from the ST_2 electrode show a remarkable drop-off which is the immediate result of the rupture in Reissner's membrane. As one would expect, response to the high frequency is not very good because this ST_2 electrode is a distance from the position of maximum activity. Here again, after the lapse of approximately two hours there begins to be a stabilization of response.

The response from the SV_3 electrode is large for the low frequencies because this is in the region of maximum activity and it becomes progressively less as the frequency is increased and the region of maximum activity moves away from the electrode position. Here again it is noticeable that following the rupture and after the lapse of two hours there appears to be a stabilization of response particularly for the frequency of 272 cps.

The noticeable thing about these curves is that, as predicted from the results of Figure 7, a more sensitive measure of the presence of injury or an injurious substance is a decrease in the dynamic range rather than a shift in sensitivity. It would appear from the curves of ST_1 that the small shifts in sensitivity and the larger shifts in the dynamic range represent injury to the region immediately below the tear in Reissner's membrane rather than to the basal turn.

CONCLUSION

Electron microscopic examination of the basilar membrane shows it to be a four-layered structure suited primarily for support of the organ of Corti in the maintenance of vibration in response to sound. It is very unlikely that it could serve as a selectively diffusing membrane because of the different types of layers and their general thickness. On the other hand electron microscopy of Reissner's membrane shows it to be a two-cell thick tissue with a squamous cell layer on the perilymphatic side that consists of very

large cells, and cuboidal cells which are thick and many in number with many microvilli extending down into the endolymphatic space. It is conceived that this membrane could very readily serve as a selectively diffusing tissue and more than likely does so.

The experiments designed to detect, by electrical recording, the spread of the deleterious effect of perilymph upon the organ of Corti following a small rupture in Reissner's membrane show no such spread within 4 hours. The changes that do occur appear to be the direct result of the Reissner's membrane tear in the second turn and not to a toxic effect upon the basal-turn organ of Corti as perilymph moves toward the basal end. This evidence seems to support further the radial-flow theory of endolymph circulation rather than the longitudinal-flow theory.

SUMMARY

In this series of experiments two procedures were carried out resulting in evidence for a radial-flow theory of endolymph circulation.

1. Reissner's membrane and the basilar membrane were examined by electron microscopy.

a. The basilar membrane is seen to consist of four layers. The basic layer divides under the outer pillar cell to include layers of longitudinal fibers above and below it. These layers of longitudinal fibers cover only the region between the outer pillar cell and the spiral ligament whereas the two groups of radial fibers extend deep into the spiral ligament.

b. Reissner's membrane is composed of two layers of cells, one on the endolymphatic side made up of cuboidal type cells with numerous microvilli while those on the perilymphatic side are flat squamous type cells extending over large areas. This membrane appears to be so constructed that it could serve as a selectively diffusing membrane.

2. Electrical recording of the cochlear potentials in the basal turn following rupture of Reissner's membrane in the second turn revealed no marked decrease in the response to high frequencies over a period of 4 hours following rupture as one would expect if Guild's longitudinal-flow theory held.

The anatomical structure of Reissner's membrane and the results of the electrical recording experiment favor a radial-flow theory of endolymph flow as proposed by Naftalin and Harrison.

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LVIII

SOME VESTIBULAR PROBLEMS IN SPACE FLIGHT

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A critical analysis is presented of the present status of our knowledge concerning the role of the nonauditory labyrinth in relation to motion sickness and other effects of the conditions to which astronauts are likely to be subjected in space travel (including weightlessness). The problems of motion sickness and spatial disorientation are discussed both in regard to the etiology of their production and to means of counteracting undesirable effects.

Only a few years ago it was claimed with confidence that man was on the threshold of flight into space. During the last two or three years, advances in engineering and space medicine have been such that the world was surprised but little, if at all, when it was announced that man had been "boosted" into space and was orbiting the earth at about 18,000 miles per hour. Such achievements mean that the pioneer astronauts are facing a complexity of factors the like of which has no counterpart in human experience. Isolation, confinement with its attendant restriction of physical activity, prolonged weightlessness, vertigo and other forms of disorientation due to strong vestibular stimulation, are stimuli against which he must be protected or for which he must be prepared. It is the object of this presentation to review our knowledge of the effects of space flight on the vestibular apparatus, i.e. on the nonauditory labyrinth. The two primary effects are motion sickness and disorientation, and it need hardly be pointed out that these may reduce the astronaut's efficiency and, indeed, jeopardize his very survival.

Defense Research Medical Laboratories, Report No. 222-40, PCC No. D50-93-10-71.

ETIOLOGY OF MOTION SICKNESS

It is sometimes forgotten that the primary cause of motion sickness is motion, although many stimuli (visceral, psychic, visual) may contribute to its incidence. Tyler and Bard[21] commented in their excellent review that: "The occasional failure to appreciate the fact that the fundamental cause of motion sickness is motion has led to some conflict of ideas." As Hemingway[11] pointed out, "The patient is sick without being aware of the cause and is therefore apt to attribute his troubles to odors, overheated compartments, visceral sensations, disagreeable sights, distasteful food or anything else unpleasant, unusual or uncomfortable which he experienced shortly before or simultaneously with exposure to motion." Time does not allow a review of all the findings which support these statements but other outstanding pertinent publications include those by Wendt,[22] Noble,[19] McNally and Stuart,[18] and more recently that of Chinn and Smith.[2]

Further evidence that motion is the significant stimulus comes from the close relationship between vestibular stimulation and motion sickness, viz.: a) susceptibility to motion sickness is eliminated in animals by removal of the vestibular organs or by dividing the VIII cranial nerves. This was first done in dogs and subsequently verified in cats;[12,18] b) ablation of the vestibular tracts in the cerebellum eliminates motion sickness in dogs;[21] c) deaf mutes with a congenital absence of the nonauditory labyrinth are known to be immune;[21] d) patients whose labyrinths have been destroyed by disease are immune.[10]

Furthermore, it is well known that patients whose labyrinthine sensitivity is being determined by caloric stimulation of sufficient strength to cause marked nystagmus often exhibit the pallor, cold perspiration, nausea and vomiting of motion sickness.

Because the nonauditory labyrinth is composed of two types of sensory receptors which are not only different in appearance but are stimulated by different types of acceleration, the relative importance of each type as a cause of motion sickness is in question. The crista of the semicircular canals are stimulated by angular accelerations whereas the otoliths are stimulated by linear accelerations; the problem, then, is one of determining whether angular or linear movements or both, cause motion sickness.

Perhaps the most emphatic recent conclusion in this regard comes from de Witt[5] who states, "seasickness is caused by over-stimulation of the otolith system." This conclusion is based mainly on the feeling that "the linear accelerations especially are greatest in the movements of a ship in rough sea. Angular accelerations are too small to stimulate strongly the sensory cells in the semicircular canals." He states that he has no record of nystagmus resulting from the motion of a vessel at sea. Shaw[20] reached the broad conclusion that "the dynamic cause of motion sickness is identical on land, sea and in the air. It is the sum of linear accelerations and de-accelerations along and around longitudinal, lateral and vertical axes." Cipriani[3] believed that when a subject is seated upright on a swing, radial acceleration is the principal vestibular stimulus. These, he stated, are of the same magnitude as the "G" changes when flying in moderately rough air. Fraser and Manning[6] using human subjects and Noble[19] using dogs, showed that with a swing at constant radius, varying the arc changed the incidence of sickness. This they also attributed to change in "G", thereby implicating the otoliths. Brunner[1] concluded that a subject is more vulnerable to seasickness in the upright position than when lying down because the otolith of the utricle is "less strategically situated for effective agitation in the recumbent position." Manning and Stewart[17] also implicated the utricle when they found that the incidence of swing sickness varied with head position. These authors arrived at conclusions identical with those of Brunner.[1] Several other authors have attributed the effect of body position on susceptibility to motion sickness to changes in orientation of the utricular macula and consequent changes in sensitivity of the otoliths.

The evidence cited suggests that linear motion is of prime importance in causing motion sickness. Closer examination, however, reveals reason to question the validity of some of the conclusions. For example, use of the cupulogram to predict susceptibility to motion sickness, as does de Witt,[5] and then to conclude that motion sickness is caused by stimulation of the otoliths seems contradictory since the cupulogram measures the sensitivity of the semicircular canals. Many authors have suggested that stimulation of the semicircular canals is of little or no importance as a cause of motion sickness because nystagmus has not been observed in seasickness. It should be pointed out, however, that motion sickness when caused by a most potent labyrinthine stimulus is regularly accompanied by unmistakable nystagmus. Rotating a subject in a horizontal plane while the head is moved

in another plane[13] frequently causes extremely large nystagmoid movements, and regularly results in the rapid onset of nausea.

Failure to observe nystagmus in some instances of motion sickness does not prove that the canals were not stimulated. It should be remembered that nystagmus is short-lived while motion sickness is long-lasting. Furthermore, weak but prolonged vestibular stimulation may not produce readily detectable nystagmus.

There is actually considerable evidence to indicate that ample stimulation of the semicircular canals by angular acceleration is the primary stimulus for inducing motion sickness. Johnson and Taylor[14] stressed this point by stating, "as the result of many experiments on the etiology of motion sickness both induced by swings and other devices, we have concluded that angular acceleration is the primary stimulus for motion sickness. In general, it can be said that we have been able to produce motion sickness under all conditions in which angular accelerations are present, and with angular accelerations alone, but we have been unable to do so with any degree of reliability under conditions in which linear accelerations alone are present. Linear acceleration, bad odors, previously existing nausea or disease may affect the incidence of motion sickness but are considered to be secondary factors." The basis upon which this statement rests consists of such findings as: a) the rapid onset of nausea, always accompanied by nystagmus, which results when a subject is rotated in the horizontal plane with accompanying head movements in another plane,[13] b) the occurrence of the highest incidence of motion sickness when the head was exposed to maximum angular acceleration rather than maximum linear acceleration (thereby implicating the semicircular canals) in a comparative study of the relative effectiveness of 2-pole and 4-pole swings in the production of motion sickness.[14] These authors further verified this finding with another laboratory device which stimulated the otoliths but not the canals.[15] Further evidence comes from clinical medicine where it is well-known that patients suffering from attacks of vertigo (with nystagmus) often complain of nausea; furthermore, caloric irrigation of the external canal during vestibular examination causes nystagmus with nausea and vomiting.

MOTION SICKNESS IN RELATION TO SPACE TRAVEL

In experimental work involving the use of aircraft to produce short periods of weightlessness, a high incidence of nausea and vomit-

ing often occurs. The author of this presentation has stressed the importance of angular acceleration as the significant fact in the occurrence of motion sickness. It should be pointed out that weightlessness results when the linear acceleration due to gravity is opposed by a linear acceleration in the opposite direction and of the same magnitude, a condition which can be produced by parabolic flight. It is the author's impression after having been exposed to about 150 periods of weightlessness of close to 30 seconds each (in a T-33 aircraft), that the absence of weight is not capable of producing nausea. The parabolic flight pattern used to produce weightlessness, however, usually imposes marked angular acceleration upon the aircraft and its occupants prior to and following the zero-G period, and any concomitant movement of the head results in multiplaner angular accelerations which are very effective vestibular stimuli[13] and the G forces undoubtedly complicate the experimental conditions, although the primary cause of sickness lies in the angular accelerations experienced. An experimental study designed to determine the effects of weightlessness should avoid such interfering accelerations. The effects of pre- and postweightlessness accelerations, however, are worthy of study since the occupants of vehicles used in such maneuvers may thereby suffer detrimental effects which could be so serious as to endanger their lives.

As for my own observations of the incidence of motion sickness in participants of zero-G flights, my conclusion is that weightlessness by itself is not nauseating. Furthermore, the types of stimulation of the nonauditory vestibular apparatus known to be most effective in the production of motion sickness are absent during the zero-G part of the parabola used on these flights. As indicated above, sickness is caused mainly by the angular accelerations resulting from unrestrained movement of the head. The head, balanced by muscular action, oscillates in at least two planes in response to the continuously changing forces imposed on it by the vehicle. Such resultant accelerations can be greatly enhanced by voluntary head movements. Consequently, I feel certain that the high incidence of nausea occurring in the zero-G flights of aircraft has been due largely to the angular accelerations occurring in the pre- and post-zero-G periods of these flights. Undesirable effects could be considerably reduced by proper instruction of the subjects prior to flight or by installation of head rests for those subjects who remain seated. As for my own sensations, I have prepared myself by lying on the floor (in large aircraft) throughout the

pre-weightlessness part of the maneuver. In this position I was careful not to move the head whether lying prone, supine, or on the side. It is considered most significant, however, that marked head movements (nodding and turning) during weightlessness did not cause any nausea and no noticeable vertigo. As soon as weight commenced to be restored when coming out of the parabola, I resumed a position of immobility on the floor. With these precautions, I did not experience any nausea at any time during such flights and this, I must conclude, was due to lack of violent semicircular canal stimulation due to head fixation in the pre- and postweightless states. Furthermore, it is recommended that when using aircraft to investigate the physiological effects of weightlessness the required parabolic flight path be entered gently from a straight and level flight path.

The conclusion that weightlessness is not nauseating seems to have been verified by the reports of Jure Gagarin and Alan Shepherd who were exposed to this condition for relatively long periods of time.

VERTIGO AS A HAZARD IN SPACE TRAVEL

In addition to the critical hazard of motion sickness which could have fatal results due to the aspiration of vomitus during weightlessness, incapacity due to vertigo may be forever present. As mentioned above, any head movement not in the plane of rotation of the vehicle constitutes the most potent labyrinthine stimulus known, at least so far as the semicircular canals are concerned. In space travel, in order to maintain the proper trajectory during initial (preweightlessness) flight, rotation of the rocket will occur, and some canal stimulation can be expected. Additional tumbling movements of the capsule toward the end of trajectory and during orbit can be expected to result in additional vestibular stimulation.

Should a space platform be established, an artificial gravity may be required to maintain normal body functions. In order to accomplish this, rotation of the platform will be necessary to produce the required centrifugal force. Therefore, it is most probable that the contained astronauts will be subjected constantly to both linear and angular accelerations while in space. The resulting effects on the nonauditory labyrinth are of serious concern not only in regard to motion sickness, but also as they concern vertigo and other disorienta-

tion effects. Compton,[4] Furey and Kraus,[7] Graybiel[10] and others have referred to such hazards of space travel. In a rotating vehicle, incapacitating effects could readily result from simple head movements (e.g. nodding movements) occurring simultaneously with trunk rotation in the plane of vehicular rotation.

If man can perform efficiently for long periods in space without the requirement for artificial gravity, the engineering problems will be greatly simplified since it will not be necessary to rotate the satellite. The recent Russian achievement of exposing a man to 89 minutes of space flight indicates no serious impairment in that period of time. However, we lack knowledge as to the effects on man of the long periods of weightlessness that are anticipated in the American astronaut program. It may well be that some degree of artificial gravity will be required. It has been pointed out that should only 0.3 G be necessary for normal physiology of the astronaut, and if man can adapt to 5 r.p.m., a satellite radius of only 11 meters would suffice. But should it be necessary to maintain a rate of rotation below 2½ r.p.m. and should one G be required, then a satellite radius of 143 meters would be necessary. In this connection, it can be noted that adaptation to frequent and violent vestibular stimulation has been demonstrated in studies involving figure-skaters.[16] The author is associated with a study of this phenomenon at the U.S. Naval School of Aviation Medicine at Pensacola and findings, some of which have just been published, show that vestibular adaptation can occur in a matter of hours.

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LIX

HISTOPATHOLOGIC FINDINGS FOLLOWING STAPEDECTOMY AND POLYETHYLENE TUBE INSERTS IN THE HUMAN

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CHICAGO, ILL.

The histopathologic findings in two ears in which stapes mobilization had been performed to improve the hearing in a case of otosclerosis were published in 1959.[1] These demonstrated the tendency for re-ankylosis to occur when fractures were made through an otosclerotic focus, and also for bony ankylosis to occur when the annular ligament had apparently been injured in the process of mobilization. The tendency for re-ankylosis to occur after simple mobilization has been amply proven by clinical experience.

The present report is based on the histopathologic findings in five ears. In two the head and crura of the stapes had been removed, the footplate fractured, and a polyethylene tube prosthesis inserted. In one of these a gelfoam pad had been inserted over the footplate. In three ears repeated mobilizations had been done and finally a fenestra made through the oval window and a vein graft and polyethylene tube prosthesis inserted.

A brief summary of the individual case reports and histopathologic findings are as follows:

CASE 1. Female patient. Diagnosis - Bilateral otosclerosis.

From the Division of Otolaryngology, University of Chicago. Presented before the American Otological Society, Inc., May 26, 1961.

The laboratory work has been supported by grants from the Central Bureau of Research of the American Otological Society, Inc., and the Deafness Research Foundation.

Expired Aug. 6, 1959, at age 76. Necropsy, Aug. 7, 1959.

History. This female patient had hearing impairment of over 40 years' duration. Hearing aid worn over eight years. General health excellent. On the insistence of her internist a stapes operation was done on the right ear on June 20, 1959. Hospitalized five days with some vertigo. Light-headedness, and loss of balance persisted until her death approximately seven weeks later.

Operation. June 29, 1959. *Right ear.* Removal of head and crura of stapes, insertion of 3½ mm polyethylene tube prosthesis, and fracture of the footplate.

Surgeon. Dr. B. W. Tanton, Vancouver, Canada.

Pre-operative pure tone audiograms for air and bone conduction, and the ninth day postoperative air conduction audiogram right ear, are shown in Figure 1.

Autopsy Report. Generalized atherosclerosis. Chronic encephalitis of the cerebellum. Right temporal bone received September 21, 1959. Fixed in formalin.

Histopathological Findings. The specimen included the middle ear and eardrum. The soft tissues show marked changes due partly to postmortem degeneration and partly to artifact, probably in fixation. The middle ear was free from inflammatory reaction. In the inner ear there was a break in the wall of the utricle, possibly artifact. There was one small spicule of bone in the vestibule which was attached to the oval window region by fine connective tissue trabeculae. Otherwise there was little evidence of proliferation within the vestibule. One large focus of otosclerosis was present at the oval window and was mainly sclerotic in character. No other foci were present. The footplate was two to three times the normal thickness and composed entirely of otosclerotic bone. It was fractured and one end displaced slightly into the vestibule. A moderately thick layer of fibrous tissue covered the middle ear surface with a thin layer of new bone in apposition to the otosclerotic bone (Fig. 2). The polyethylene strut had been covered by an extremely thin layer of connective tissue and epithelium. It extended from the incus to the fibrous layer overlying the footplate by which it was apparently well

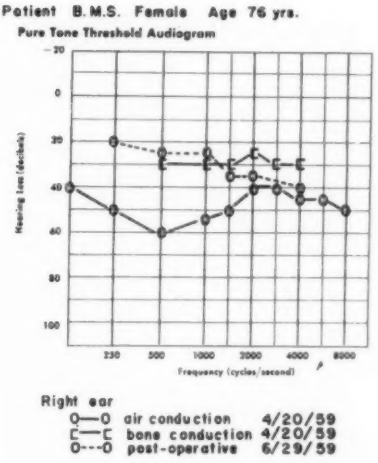


Fig. 1.—Case 1. Right ear. Pre-operative pure tone threshold audiogram for air and bone conducted sounds shown by solid lines, and postoperative air-conduction thresholds by broken line.

supported in position (Fig. 3). Regeneration of bone in fissures and along the footplate are illustrated in the figure.

Comment. The footplate of the stapes was composed almost entirely of otosclerotic bone. The fragments showed fairly wide separation in some areas with moderate depression into the vestibule. There was evidence of active new bone formation in apposition to the old otosclerotic bone. The strut was in good position, a fairly thick layer of fibrous tissue had formed in the niche and the inner ear was free from inflammatory reaction and from evidence of traumatic injury. At the forty-seven day period an excellent functional result could be predicted. Two main questions may be raised by the histopathologic findings; the possibility of refixation and the degree of protection to the inner ear.

In view of the active osteogenesis in this case and the tendency for regeneration of bone when a thick otosclerotic footplate is fractured reankylosis may take place eventually although it would prob-

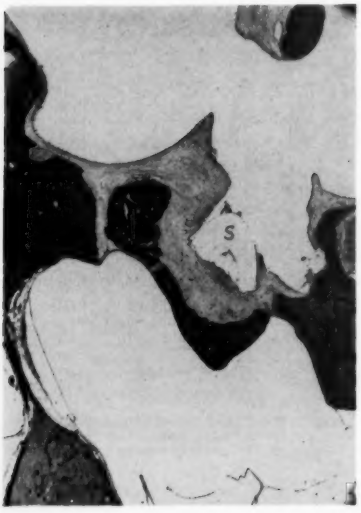


Fig. 2.—Case 1. Right ear. Photomicrograph of section through the stapes footplate which is depressed into the vestibule slightly. The footplate is thick and composed of otosclerotic bone. The break in the footplate is shown at higher magnification in Figure 3. The position of the strut (S) is clearly indicated, separated from the footplate by a thick pad of fibrous tissue.

ably take many months to develop. The position of the strut and the thickness of the fibrous tissue layer beneath it in the niche suggest a high degree of protection to the vestibule.

CASE 2. Male patient. Specimens and history received from the Otologic Medical Group of Los Angeles.

Surgeon. Dr. Howard P. House.

History. Patient first seen in June 1958 at age of 81 with history of gradually progressive hearing loss for 50 years.

Pre-operative AC and BC pure tone thresholds and the postoperative A.C. pure tone audiogram made three weeks after operation are

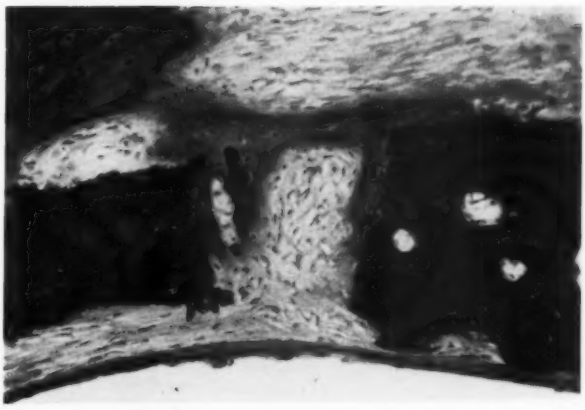


Fig. 3.—Case 1. Right ear. High power magnification to show the regeneration of bone in the gap in the footplate. This had occurred in 47 days.

shown in Figure 4. Expired, following a heart attack, Feb. 21, 1960, 27 days after the operation.

Operation. January 25, 1960. Right stapes operation. Bipolar fixation noted. Head and crura removed. Footplate shattered with needle. A 4 x 5 mm piece of gelfoam placed over the footplate and a 4½ mm polyethylene strut inserted.

The temporal bones and brain were received on March 4, 1960, fixed in formalin.

Histopathologic Findings. This was bilateral otosclerosis. Only the right ear had been operated and will be described.

Right Temporal Bone. Specimen received in good condition.

Early post-mortem degenerative changes were present and artifacts due to fixative or processing were apparent in the soft tissue structures. Middle ear and inner ear were free from proliferative changes except at the region of the oval window. A defect was

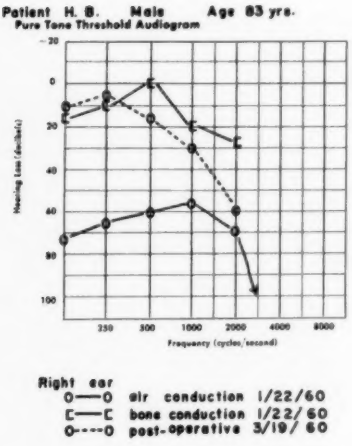


Fig. 4.—Case 2. Right ear. Pre-operative pure tone threshold audiograms for air and bone conducted sounds are shown by solid lines. The broken line shows the air conduction audiogram at 25 days after operation.

present in the wall of the utricle but there was no conclusive evidence to indicate whether or not it was an artifact.

There was one large otosclerotic focus at the oval window region. A small shallow focus was also present at the anterior margin of the internal meatus, in the enchondral layer.

The footplate was free of otosclerosis except anteriorly. The focus extended beyond the anterior crus superiorly and inferiorly along the margin for a short distance and was mainly sclerotic in character. The footplate was fractured into several pieces, one spicule extending into the vestibule in apposition to the strut, the end of which extended well into the vestibule but did not contact the otoliths. The tip of the strut was covered by a thin layer, apparently connective tissue fibers. The portion in the middle ear was partly surrounded by a relatively thick layer of connective tissue while one side was covered only by a faintly stained thin layer, apparently of epithelium.

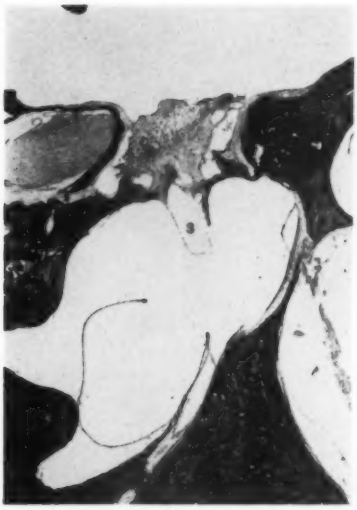


Fig. 5.—Right ear. Photomicrograph of section through the upper central part of the footplate. The fractured footplate was composed of normal bone at this level, but was otosclerotic along the upper and anterior margin where ankylosis had occurred.

Remains of gelfoam are shown in the niche of the window. The tip of the strut (arrow) projected freely into the vestibule, depressing a fragment of footplate with it. A faint layer of connective tissue covered the strut.

Remnants of gelfoam remained in the niche of the window (Figs. 5 and 7).

Comment. The footplate was composed mainly of normal bone, with otosclerosis at the anterior and posterior ends.

One fragment had been displaced into the vestibule alongside the strut, both of which projected well into the vestibule. At 27 days after operation there was no clear evidence of inner ear damage or reactive labyrinthitis. A thin layer of cells covered the polyethylene strut both in the vestibule and in the middle ear. The histopathologic findings in this case suggest certain comments. The projection

Fig. 6.—Case 2. Right ear. Photomicrograph of section slightly lower than Figure 6. The position of the strut is clearly indicated by the thin layer of connective tissue which had ensheathed it. The inner ear was free from inflammatory reaction. The defect in the wall of the utricle and depression of the saccule are not explained and may be artifact.

of the strut into the vestibule should tend to prevent reankylosis and therefore give a more permanent result. The question which arises however is whether the extension of the strut through the limiting fibrous tissue wall of the window might impair the degree of protection to the vestibule from infection or trauma.

Case 3. Male patient. Case record and specimens received from Otological Group of Los Angeles.

Surgeon. Dr. Howard P. House.

Diagnosis. Bilateral otosclerosis.

History. Progressive hearing loss of over 15 years' duration. Strong family history of hearing loss. No vertigo or tinnitus.

Surgery Performed. Otologic Medical Group, Los Angeles.

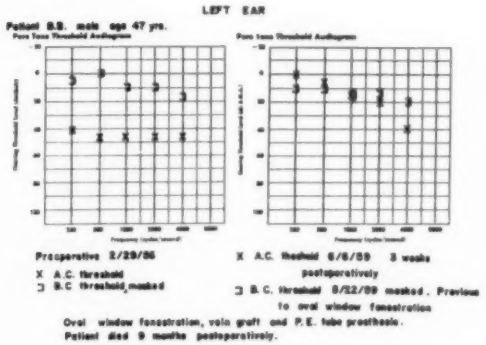


Fig. 7.—Case 3. Left ear.

Right Ear. April 21, 1956. Stapes mobilized through the capitulum.

Ligamentous tear and escape of perilymph, vertigo on the operating table. At three weeks had a 3 db gain by AC and an 8 db *drop* for BC.

Hearing returned to pre-operative levels.

November 10, 1956. Stapes mobilized at the footplate with Grade 2 mobility and vertigo on the operating table. At three weeks the AC hearing level was at 22 db. Two and one-half years later and eight and one-half months prior to his death the hearing level averaged 13 db for speech frequencies.

Left Ear. March 5, 1956. Stapes mobilization via the capitulum.

Improvement at three weeks to the 28 db level. Regressed in four months to the 38 db level.

November 10, 1956. Remobilization via the capitulum. Grade 3 mobility and vertigo on the table. Thirteen db gain at operation. Twenty db gain at three weeks. Regression to pre-operative level in eleven months.

Fig. 8.—Case 3. Photomicrograph of section No. 335 left, near the upper margin of the oval window. A fragment of footplate (F.P.) is shown extending from the base of the anterior crus, which was densely ankylosed to the anterior and superior rim of the window.

The wall of the vein which ensheathed the tip of the strut (S) is shown within the vestibule.

February 10, 1958. Second remobilization via the capitulum. Grade 3 mobility with vertigo on the table. Ten db improvement on the table and 15 db at three weeks. In two months regression had occurred to the pre-operative level.

May 25, 1959. Fenestration of oval window. Vein graft and 3½ mm polyethylene strut. This appeared to be an anterior crural fixation. Posterior two-thirds of footplate removed with a needle. Hearing level at 13 db average for speech frequencies at three weeks after operation. No further tests available. Death February 14, 1960, eight and one-half months after operation, from a heart attack.

Pre- and postoperative audiograms shown in Figure 8.

The temporal bones and brain were removed 36 hours after death and received March 1, 1960, fixed in formalin.

Histopathology. This was bilateral otosclerosis. Only the left ear had undergone fenestration of the oval window, and will be described in this report.

Left Ear. The specimen contained the middle ear as well as the nerve within the internal meatus.

Soft tissues showed changes due partly to postmortem degeneration and partly to artifact in preparation. Cochlear nerve, spiral ganglion and stria vascularis were in good condition. Corti's organ compressed with Reissner's membrane partly adherent and condition of hair cells could not be determined accurately. The vestibule showed no evidence of inflammatory reaction. The otoliths appeared normal. The labyrinthine capsule contained extensive otosclerosis. The main focus at the oval window was partly sclerotic, but markedly vascular in parts. A small focus was present at the anterior border of the internal meatus, also vascular and fibrous. One other large focus of the sclerotic type was present in the anterior part of the cochlear capsule. "Blue mantels" were prominent and extensive around the semicircular canals. The stapes was mostly absent. A portion of footplate attached to the base of the anterior crus was still present and clipped medially. New bone was forming and had produced early extensive refixation of this fragment to the otosclerotic rim of the window (Figs. 8, 9A and 9B). The window was otherwise filled with fibrous tissue in which were many vascular spaces and the vein graft which surrounded the tip of the strut. The position that the polyethylene strut has occupied was clearly evident. It projected into the vestibule beyond the limits of the window and was enveloped by the thin vein. The walls of the vein were distinguishable by the presence of elastic tissue fibers which stained well with Verhoff's elastic tissue stain. The strut was in good position. The posterior inferior rim of the window was free from otosclerosis. Some spicules of old bone were present in the fibrous tissue in the anterior part of the niche. There was some new bone in apposition to the old otosclerotic rim (Fig. 9), but it did not appear to encroach on the vein graft as it enveloped the strut. In the middle ear the strut was covered by an extremely thin layer of tissue on its inner surface while on its outer surface connective tissue covered by epithelium could be seen.

The elastic tissue stain demonstrated the presence of elastic tissue fibers in the thin-walled covering of the medial portion of the strut (Figs. 9A and 9B) as it lay in the vestibule.

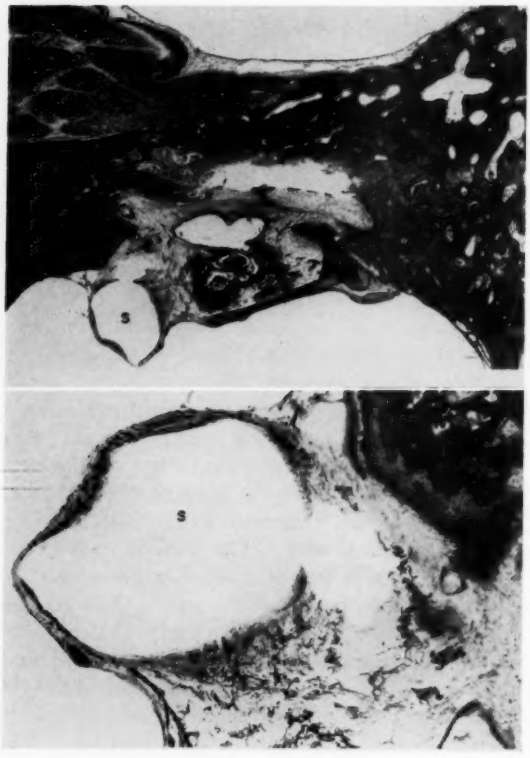


Fig. 9A.—Photomicrograph of Section 341 left, stained by Verhoff's elastic tissue stain shows the extensive reankylosis of the fragment of footplate to the otosclerotic rim. The wall of the vein surrounding the strut (S) is shown at higher magnification in Figure 9B.

Fig. 9B.—Photomicrograph X 130 of the wall of the vein. Elastic tissue fibers were still evident in the thinned part of the vein surrounding the tip of the strut (S).

Comment. The *right ear* is not presented here since the operation consisted of mobilization and revision and will be considered in a separate report. The extent of the otosclerosis was however similar to that in the left ear. The stapes was present, the footplate fractured, with some gaps between fragments, and mobility apparently still maintained.

The *left ear* had undergone four operative procedures, three of them mobilizations and the fourth a stapedectomy. The vestibule was free from inflammatory reaction except at the region of the oval window.

The strut extended into the vestibule where the tip was ensheathed by the thin walled vein, and a few elastic fibers could be seen in this part of the vein graft.

At eight and one-half months the major part of the oval window niche was occupied by fibrous tissue, vein and strut. The hearing test unfortunately had been made nearly eight months before death and it is not recorded if any regression had occurred.

Some of the questions which arise are: while the projection of the strut into the vestibule provides improvement in function and probably permanent patency, would the new bone formation around the strut in the window progress enough to reduce the efficiency? Also would the degree or protection afforded against infection and trauma be impaired? In this case the findings at eight and one-half months indicate excellent prospect for maintenance of a functioning window. The persistence of the wall of the vein around the tip of the strut, although quite thin, gives some reassurance as to its protective capacity.

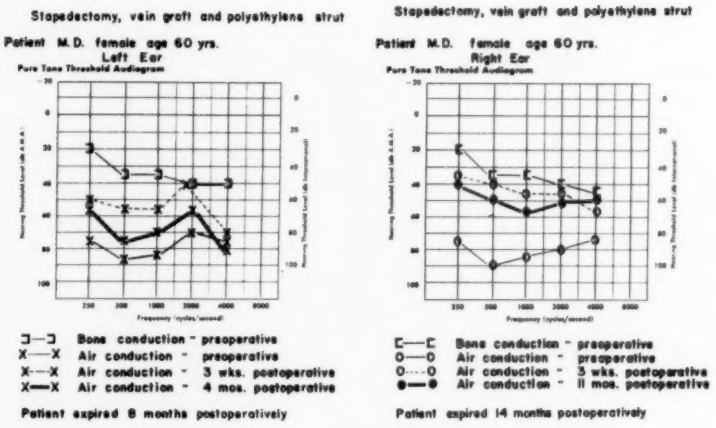
CASE 4. M.D., female. Case record and specimens received from Otologic Medical Group of Los Angeles.

Surgeon. Dr. Howard P. House.

Diagnosis. Bilateral otosclerosis.

Expired August 21, 1960, at age 60. Cardiac failure. Hypertensive cardiovascular disease.

History. Gradually progressing hearing loss bilaterally for more than 20 years. Had worn a hearing aid for 15 years.



Figs. 10A and 10B.—Audiogram.

Surgery. Left Ear. November, 1957. Stapes mobilization. Footplate needled and shattered. Improvement of 12 db was lost at four months.

February, 1959. Revision. Bipolar otosclerosis noted. Crura removed. Footplate shattered. Polyethylene strut inserted. Improvement from the 82 db level to the 65 db level.

January, 1960. Second Revision. Solid otosclerotic fixation. Footplate removed by drilling. Vein graft and polyethylene strut inserted. The hearing levels for AC and BC four months before surgery, and for AC at three weeks and at four months after surgery are shown in Figure 10A. The gain of 30 db at three weeks postoperative had regressed to 13 db for speech frequencies at four months. Patient expired August 21, 1960, eight months after the final operation on the left ear.

Right Ear. October, 1958. Mobilization of stapes at the footplate using needle and chisel. A 20 db hearing improvement had disappeared at three months.

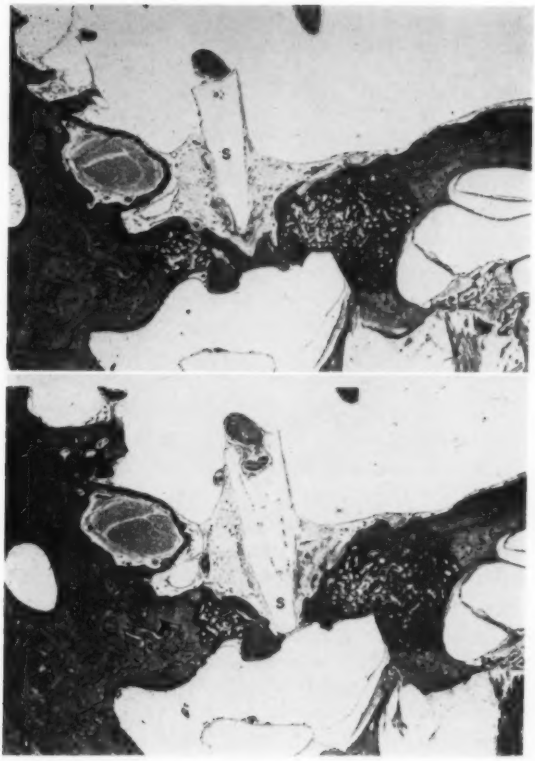


Fig. 11A.—Photomicrograph of Slide No. 295. Left. The position of the strut (S) is clearly indicated. The fenestra has been filled by a layer of dense lamellar bone at this level.

Fig. 11B.—Case 4, left ear. Photomicrograph of Section No. 305. Left. At this level the fenestra is limited to the area of the tip of the strut (S) by the surrounding new compact lamellar bone extending from the otosclerotic margins.

Fig. 12.—Case 4, left ear. Photomicrograph of section No. 305 left X 100. This shows elastic tissue in the walls of the vein graft (Verhoff's stain). At the tip of the strut the elastic tissue is no longer present and the vein wall has fused with a layer of fibrous tissue from the endosteum..

June, 1959. Revision. Solid otosclerotic fixation found. Half to a third of the footplate removed by drilling. Vein graft and polyethylene strut inserted. The hearing levels for AC and BC before operation, and for AC at three weeks and at eleven months after operation are shown in Figure 10B. Regression of 10 db had occurred. Patient expired 14 months after surgery on right ear.

The hearing levels for air and bone conduction before surgery and for air conduction after surgery are shown in Figure 12. Expired fourteen months after surgery. The final hearing test, made three months before death, showed further regression to the 52 db average for speech frequencies. The temporal bones and brain were removed eight hours after death and received September 7, 1960, fixed in formalin.

Daley, left ear.

Histopathology. The specimen contained the middle ear and the nerves in the internal acoustic meatus. The bone was in a good state of preservation. Soft tissues showed early postmortem degenerative changes.

There was adherence of Reissner's membrane to Corti's organ and compression due to artifact, possibly in the fixation process, which precluded accurate hair cell studies. The stria vascularis, spiral ganglion and nerve fibers were apparently normal in extent and numbers. The middle ear was normal except for the oval window niche region. The vestibule was free from any gross proliferative changes or evidence of injury but some microscopic particles of bone dust were adherent to the wall of the utricle, in which slight thickening and vascular congestion was apparent.

There was one large focus of otosclerosis only. This had surrounded the oval window. Part of the focus was moderately sclerotic but much of it was markedly vascular (Figs. 11A and 11B). Two small remnants of footplate were present, apparently from the base of the posterior crus. The strut had been in place surrounded by vein graft and some fibrous tissue. The most striking feature was the extensive deposit of new bone, mainly of the compact lamellar type which had encroached on the lumen of the niche from all sides and reduced the fenestra to the width of the strut at its tip. Otosclerotic bone extended into this compact bone so that the line of demarcation was not clearly discernible in many areas.

The walls of the vein contained only remnants of elastic fibers at the tip of the strut. At this point the wall of the vein was fused with a thin connective tissue layer from the endosteal margins of the window (Fig. 12).

The strut in its middle ear part was covered by a layer of delicate connective tissue and epithelium on its outer and inner surfaces.

Comment. In this ear the strut had been in excellent position and the vein graft preserved except for some atrophy of elastic fibers at the tip of the strut. The inner ear had apparently suffered no injury from the three operative procedures.

The striking feature had been the extensive regeneration of bone in the niche to the point of limiting the fenestra to the area of the tip of the strut. Impairment of function due to increased impedance could be anticipated under this circumstance and is apparently confirmed by the audiogram although the hearing level at four months might not indicate the thresholds at the time of death eight months after operation.

Histopathology. Right Ear. The specimen contained the middle ear and part of the nerve in the internal meatus. The bone was in good condition but soft tissues showed compression changes attributable to artifact. Nerves, ganglion cells and stria vascularis were well preserved. Corti's organ was compressed and hair cells not identifiable due to artifact. The middle ear was free from inflammatory changes. The vestibule contained fine bone dust particles under the rim of the window incorporated in vascular new bone extending from the focus in the niche (Fig. 13A).

The otoliths were intact except for a defect in the wall of the saccule, possibly artifact.

There was an extensive single focus of otosclerosis at the oval window region. Blue mantles were absent in the labyrinthine capsule. The focus was markedly vascular in nearly all areas. The basal part of the posterior crus was still present, extremely thick, otosclerotic and densely ankylosed to the posterior rim. The anterior part of this crus was composed of a layer of dense new bone, partly lamellar in type, which was part of a wall of new bone that was present in the niche surrounding the strut.

The striking feature of the repair process was the filling up of the niche with new bone. This was mainly lamellar in type but was continuous with the otosclerotic rim of the niche and the posterior crus without a clear cut demarcating border. The appearance suggested that there had been rapid osteogenesis filling the niche with compact lamellar bone into which otosclerotic bone was now extending (Figs. 13A and 13B).

The walls of the vein graft were clearly distinguishable by the elastic fibers shown by Verhoff's elastic tissue stain. The end of strut

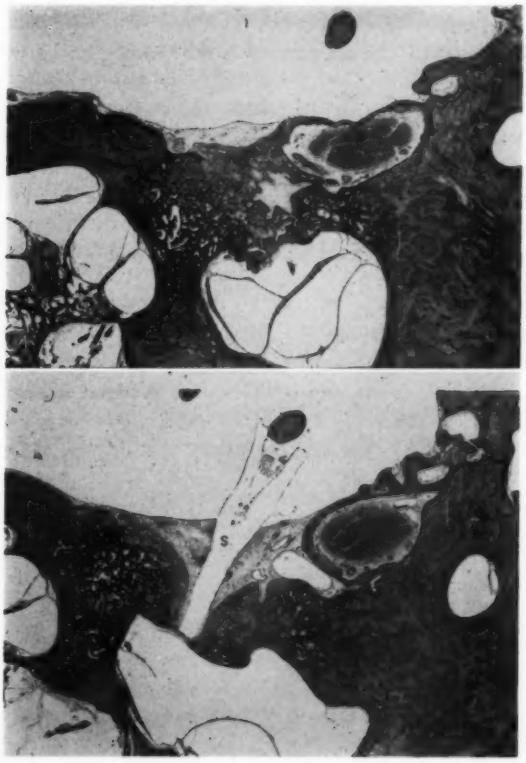


Fig. 13A.—Case 4. Right ear. Photomicrograph of Section 260 at the upper level of the oval window. The niche has been filled with new compact bone which is not clearly demarcated from the otosclerotic focus. Some spicules of old bone have lodged beneath the margin of the oval window and have been incorporated into the new bone filling the niche.

Fig. 13B.—Case 4. Right ear. Photomicrograph of Section 300. The position occupied by the strut (S) is indicated. The fenestra has been reduced by formation of compact lamellar bone to the width of the strut and the thin wall of the vein graft.

was covered by a layer of fibrous tissue in which only remnants of elastic fibers could be identified.

The soft tissue communication with the vestibule was therefore limited to the area of the tip of the strut.

The part of the strut in the middle ear was covered by a delicate layer of connective tissue fibers and epithelium.

Comment. The strut and vein graft were in good position. The vein graft was preserved except for atrophy of elastic tissue fibers at the tip of the strut. There was no evidence of inflammatory reaction around the strut.

The striking feature was the extensive filling in of the oval window niche by bone. The area of the functioning window was reduced to the area of the tip of the strut. This had occurred in slightly more than one year. The hearing levels and the air-bone gap at one year (Figs. 10A and 10B) apparently reflect the degree of impedance offered at the oval window.

COMMENT

Some of the questions for which the answers might be sought in the histopathologic findings are as follows:

Is there evidence of foreign body reaction around the strut? Are there any signs of reaction, inflammatory or irritative, within the vestibule? Is there evidence of trauma to the sensory epithelia?

Are there features which might shed light on the occurrence of inner ear damage that has been known to occur in the occasional case —either as an early complication of the operation, or as a late complication of an acute middle ear inflammation, or following exposure to sudden pressure change, or as a loss of function of unknown etiology.

These five cases illustrate only a minimal degree of inflammatory reaction around the polyethylene strut as indicated by proliferation of connective tissue.

The one case in which the unprotected tip of the strut reached into the vestibule showed no reaction.

In Case 1 the tendency to osteogenesis and eventual refixation when a thick otosclerotic footplate is fractured but left in place was already evident at less than two months.

The shattering of the normal part of the footplate as shown in Case 2 has produced little osteogenesis at this stage.

The projection of the strut into the vestibule raises the question as to whether the protection of the inner ear against entry of infection or trauma might be weakened.

Case 3 exhibited a widely patent fenestra at eight and one-half months, a stage when osteogenesis is probably near its maximum. The end of the strut which projected into the vestibule had the enveloping wall of the vein to give added protection against invasion by infection, also probably against trauma.

Case 4 exhibited conditions which were almost identical in both ears. The oval window niche had filled up with new bone until it closely surrounded the strut and vein.

The walls of the vein were still demonstrable although elastic fibers had mostly atrophied in the part surrounding the tip.

These ears represent a type well known clinically in which at revisions the growth of new bone tending to obliterate the niche has been evident. Increased impedance to sound transmission despite a well placed graft and strut seems explained by the encroachment of new bone as demonstrated in these two ears. The findings suggest that in this type of case in the presence of good bone conduction a fenestration of the horizontal canal might be the procedure of choice.

SUMMARY

Histopathologic findings are presented in five ears in which a partial or total stapedectomy had been carried out.

In two ears, removal of the crura and head was followed by insertion of a gelfoam pad in both and polyethylene strut in both.

In three there had been a partial or subtotal removal of the footplate followed by insertion of vein graft and polyethylene tube strut.

The polyethylene was tolerated by the tissues in all cases with only minimal signs of reaction.

The vein grafts were preserved in all cases. Partial atrophy of elastic tissue fibers occurred about the tips of the struts.

Gelfoam had been incompletely absorbed at five weeks and fibrous connective tissue reaction was still evident at five weeks.

While each case represents a different set of conditions each has added essential information relative to the success of fenestration of the oval window.

Case 3 exhibits a widely patent fenestra at eight and one-half months, a stage when osteogenesis is probably near its maximum. The end of the strut which projects into the vestibule has the enveloping wall of the vein to give added protection against invasion by infection, also probably against trauma.

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These ears represent a type well known clinically in which at revisions the growth of new bone tending to obliterate the niche has been evident. Increased impedance to sound transmission despite a well placed graft and strut seems explained by the encroachment of new bone demonstrated in these two ears.

950 East 59th St.

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1. The history and temporal bones of case No. 1 were furnished by Dr. B. W. Tanton of Vancouver, Canada.

2. The histories and temporal bones from cases 2, 3 and 4 were furnished by the Otological Medical Group of Los Angeles, Cal.; Surgeon: Dr. Howard P. House.

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1. Lindsay, John R., Hilding, Anderson C., McLaurin, James W., Keeler, Nelson S., and House, Howard M.: Histopathologic Changes Following Fenestration and Stapes Mobilization. Tr. Am. Acad. Ophth. and Otolaryng. 63:187, 1959.

LX

A CLINICAL AND LABORATORY EVALUATION OF POLYETHYLENE TUBING IN MIDDLE EAR SURGERY

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AND

HELEN BURN, M.A.

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In 1960 Bellucci and Wolff[1] in a well-documented paper described extensive fibrosis and occasional osteogenic reaction of the vestibule and cochlea in cats following experimental stapedectomy and reconstruction using polyethylene struts and either gelfoam or vein grafts.

These findings were so much in variance with our clinical experience that twelve months ago a study was undertaken to determine whether this process would also occur in monkeys similarly treated.

Seven animals (Rhesus and Cynamolgus) were used, the procedure and duration is indicated in the following tables.

I. Stapedectomy and Polyethylene Strut

	Right Ear	Left Ear
	Gelfoam on Window	Gelfoam Packed in Vestibule
M 14	3 Mo.	2 Mo.
M 15	3 Mo.	3 Mo.
M 16	1 Mo.	1 Mo.

From the Division of Otolaryngology, University of California Medical School, San Francisco 22, California.

II. Stapedectomy and Polyethylene Strut

	Right Ear	Left Ear
	Gelfoam on Window	Vein Graft on Window
M 17	4 Mo.	4 Mo.
M 18	4 Mo.	3 Mo.
M 19	3 Mo.	3 Mo.
M 20	1 Mo.	1 Mo.

TECHNIQUE

The animals were anesthetized with intravenous Nembutal Sodium® and the head shaved. The inferior surface of the bony external auditory canal was exposed through an infra-auricular incision (Fig. 1) and removed with small rongeurs. In all but one instance the filmy drum membrane was perforated during exposure of the middle ear. The stapedius tendon and incudostapedial joint were severed and the entire stapes removed (Fig. 2).

Initially, No. 90 polyethylene tubing was tried but because of a marked disproportion between the lenticular process of the incus and the tube orifice later cases were done with No. 50.

The perforation in the repositioned drum was covered with gelfoam and the incision sutured with No. 0000 chromic catgut. Two injections of penicillin were given postoperatively.

At intervals of one to four months the animals were anesthetized, exsanguinated and perfused with saline followed by 10% neutral formalin.

The temporal bones were decalcified, imbedded in celloidin, serially sectioned, and stained with hematoxylin and eosin. No hearing tests were done and all conclusions are based on histological evidence.

RESULTS

All seven animals survived without clinical evidence of infection.

There was microscopic evidence of minor neutrophilic infiltration of the middle ear (Figs. 3 and 4) in four of ten gelfoam ears, and two

Fig. 1.—Incision exposure of the bony external auditory canal and the view of tympanic membrane with the external auditory canal partly removed.

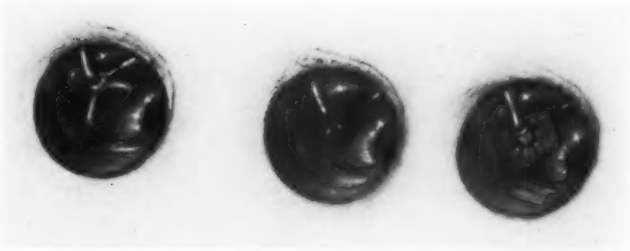

Fig. 2.—The technique of the vein graft in the Rhesus monkey.

of the four vein graft ears. One of the latter also had microscopic mastoiditis.

The vestibule and cochlea in each case was entirely free from infection and fibrosis.

Varying degrees of degeneration were seen in the organ of Corti and this was attributed to "acoustic trauma" following forcible removal of the stapes and manipulation in the oval window area (Fig. 5 and Fig. 6).

Several struts had shifted from their original position; however, the fibrous reaction around the polyethylene was similar in the gelfoam and vein graft ears (Fig. 7 and Fig. 8), and no difference could be seen between one- and four-month specimens.

Fibrosis in the oval window was much more extensive when gelfoam was used (Fig. 9) as compared to vein grafts (Fig. 10).

Packing gelfoam in the vestibule failed to stimulate fibrosis in this area even though particles resembling gelfoam were seen in the cochlea of one such specimen (Fig. 11) again without fibrosis.

One strut was found entirely within the vestibule surrounded only by a thin layer of endothelial cells (Fig. 12) after four months and with no other evidence of reaction in spite of a small amount of purulent exudate on the tympanic side of the oval window membrane.

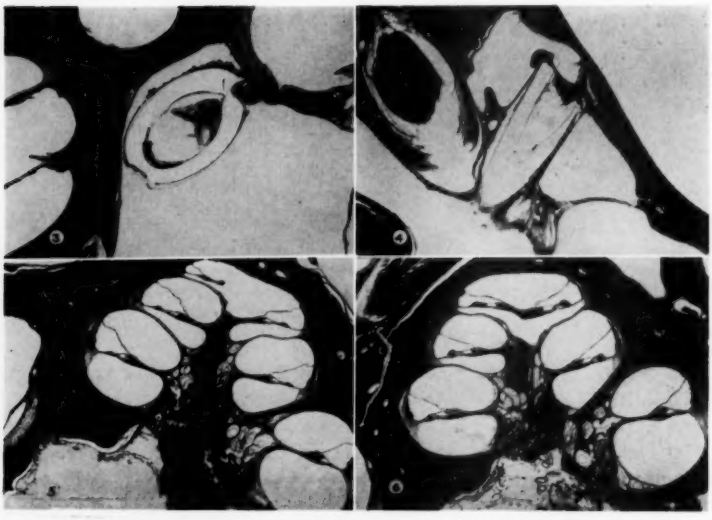

Fig. 3.—Polyethylene strut in the middle ear three months after implantation showing small collection of purulent cells in the center of the strut.

Fig. 4.—Polyethylene strut showing usual fine network of fibroblasts around the outside of the strut 3 months after implantation.

Fig. 5.—Cochlea four months after stapedectomy and gelfoam polyethylene reconstruction.

Fig. 6.—Cochlea four months after stapedectomy and vein graft polyethylene reconstruction.

Significant absorption occurred in two of the four veins without compromise to the vestibule or cochlea.

Two findings of considerable clinical interest were noted. In four of the 10 gelfoam specimens *new bone* formation was found at the oval window in the fibrous membrane (Fig. 13 and Fig. 14), whereas none was seen in the four vein ears.

In addition to the one strut found in the vestibule (Fig. 12), a second was seen perforating the oval window membrane (Fig. 15) and separated by a single cell layer in another (Fig. 16).

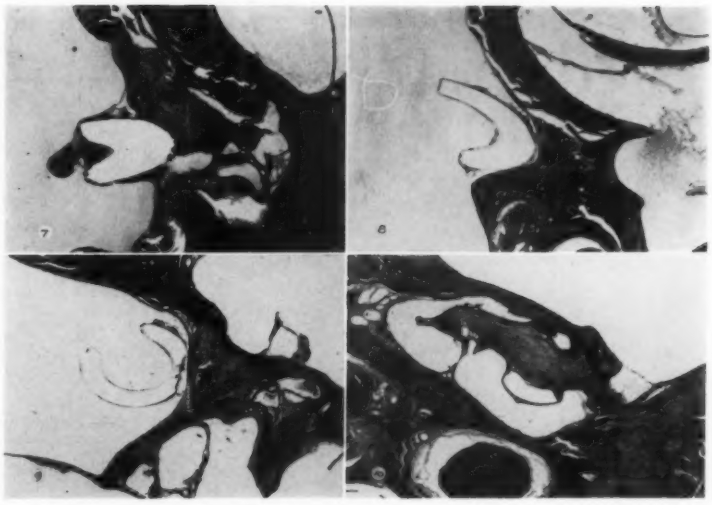

Fig. 7.—Polyethylene strut and vein graft at one month.

Fig. 8.—Polyethylene strut at the oval window niche two months after stapedectomy with gelfoam placed in the oval window and vestibule.

Fig. 9.—Oval window niche three months following stapedectomy with gelfoam placed over the oval window. Polyethylene strut has slipped slightly.

Fig. 10.—Oval window niche four months following stapedectomy. The tip of the polyethylene strut is against the vein graft.

CLINICAL STUDY

1500 stapes operations were reviewed and the 417 in which polyethylene was used were studied in detail. No followup was available in 29 cases, and these were not included. The remaining 388 were divided as follows:

205 Fragmentation of the stapedial footplate, gelfoam, and polyethylene strut. (House technique)

183 Stapedectomy, vein graft and polyethylene strut. (Shea technique)

The results are tabulated on the following page.

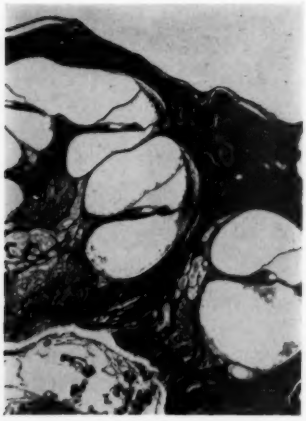

Fig. 11.—The cochlea two months following stapedectomy and packing of gelfoam into the vestibule.

388 Pts.—Closure of Air Bone Gap

	P.E.S. & Gelfoam		P.E.S. & Vein	
	Pts.	%	Pts.	%
Overclosed	83	40.4	116	63.4
Closed to 10 db	85	41.4	46	25.1
	168	81.9%	162	88.5%

388 Pts.—Sudden Severe Hearing Loss

	P.E.S. & Gelfoam		P.E.S. & Vein	
	5 Pts.	2½%	2 Pts.	1.1%
Immediate	2		0	
Delayed	3		2	
Salvaged	1		1	
	4	2.0%	1	0.5%

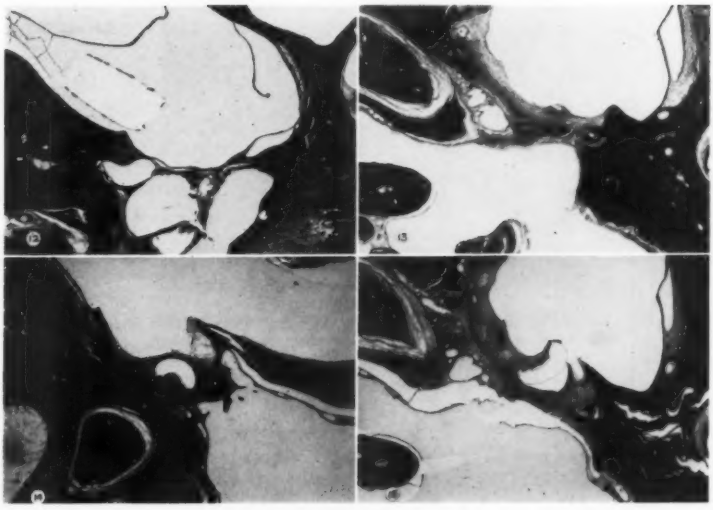

Fig. 12.—Polyethylene strut in the vestibule four months following stapedectomy with gelfoam over the oval window. Small purulent collection is seen on the middle ear side of the oval window.

Fig. 13.—Oval window one month following stapedectomy and gelfoam reconstruction. Note the new bone formation in the scar tissue which has replaced the gelfoam.

Fig. 14.—Oval window niche one month following stapedectomy and gelfoam reconstruction. Note the tip of the polyethylene strut within the scar tissue, which also contains new bone formation.

Fig. 15.—Perforation of the fibrous tissue membrane over the oval window by the polyethylene strut one month following stapedectomy with gelfoam reconstruction. Note the area suggesting new bone formation in the scar tissue.

388 Pts.—Sudden Loss But Not to Pre-Op. Level

	P.E.S. & Gelfoam		P.E.S. & Vein	
	Pts.	%	Pts.	%
	3	1.5	4	2.2
Salvaged	0		1	
	3	1.5%	3	1.6%

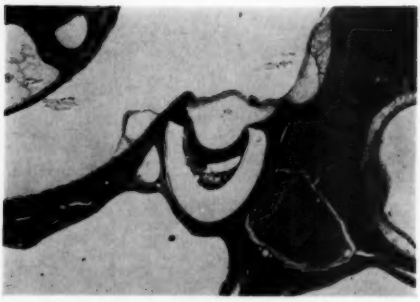

Fig. 16.—Oversized polyethylene strut at the oval window niche three months following stapedectomy with gelfoam reconstruction. Note the thinness of the fibrous tissue between the polyethylene strut and the vestibule. Small purulent collection is seen within the polyethylene strut.

It would appear that better hearing levels are obtained with vein grafts than when gelfoam is used, and that the principal complication with gelfoam is related to inadequate labyrinthine protection as evidenced by the four perforations in the following table:

388 Pts.—Cause of Sudden Hearing Decrease

	Gelfoam Pts.	Vein Pts.
Footplate Perforated Strut in Place	2	--
Footplate Perforated Strut Slipped	2	--
Strut Slipped No Perforation	1	1
Labyrinthine Hydrops	1	4
Purulent Labyrinthitis	--	1
Fibrous Closure Oval Window	2	--
	8	6

All strut dislocations and perforations occurred spontaneously in the gelfoam procedures. The one instance with a vein graft followed a severe fall.

The three patients listed as "salvaged" are of interest. In one this was accomplished by replacing a longer strut on the vein graft of the patient with the head injury. A second vein graft achieved normal hearing when the strut was removed promptly following a severe labyrinthine hydrops on the third postoperative day. The third patient developed a sudden drop in hearing following the use of gelfoam and fragmentation of the footplate. Vein graft revision was successful.

In addition to these there are thirteen gelfoam patients and two vein graft patients who had good initial results but are now showing a progressive hearing decrease suggesting oval window closure.
oval window closure.

SUMMARY AND CONCLUSIONS

1. An experimental comparison of gelfoam vs. vein graft in polyethylene strut stapedectomy on monkeys is reported and compared with a detailed analysis of similar procedures on 388 patients.

2. The animal series, although small (14 ears), suggests the following:

A. Polyethylene alone is well tolerated and essentially non-reactive.

B. There is no significant difference in the fibrosis around the polyethylene whether vein or gelfoam is used.

C. There was no significant difference observed in the fibrosis around the polyethylene between one and four months.

D. Both gelfoam and vein grafts create an effective barrier against otitis media.

E. No fibrotic reaction was observed in either vestibule or cochlea.

F. Gelfoam packed into the vestibule does not produce a fibrous reaction.

G. Gelfoam over the oval window produces more fibrosis than vein grafts and is less resistant to strut perforation.

H. Four instances of new bone formation at the oval window were seen when gelfoam was used, none with vein grafts.

3. The clinical analysis of 388 patients indicates:

A. Better hearing levels are obtained with grafts than with gelfoam.

B. Gelfoam offers poorer resistance to strut perforation.

C. A higher incidence of oval window closure is present in the gelfoam series.

The authors thank Miss Anne Kieffer and Miss Marcia Rew for expert assistance in experimental surgery and preparation of sections.

UNIVERSITY OF CALIFORNIA
MEDICAL CENTER

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LXI

THE RELATION OF AIR CONDUCTION AUDIOMETRY TO OTOLOGICAL ABNORMALITIES

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For the past four years, the Subcommittee on Hearing in Children, of the Committee on Conservation of Hearing of the American Academy of Ophthalmology and Otolaryngology, has been concerned with a long-term nationwide study of hearing problems in children, the objectives of which have been previously described.[1,2] Part of a current study is concerned with the relation of air conduction audiometry to otologic abnormalities.

The data in this paper are based on the first otoscopic examination of 4067 children, age 5 to 14 years, in which there was a concurrent reliable hearing level determination. Of these children, 2891 were classed as otoscopically normal, and 629 as abnormal. The examination of 547 children in this group could not be completed because of cerumen in the auditory canal of one or both ears. Removal of cerumen to facilitate examination was regarded as treatment, and therefore not permitted by a ruling of the Pittsburgh School Medical Service.

The accuracy of the audiometry and the standards of acoustic environment have been reported elsewhere.[1,2] It will be recalled that an acoustic environment was provided, in which hearing levels could be measured to minus 30 db with linearity.

In the interest of consistency and objectivity, certain limitations were placed on the examining otolaryngologist. Three otolaryngologists, each of whom had been in practice for ten years or more, and all certified by the American Board of Otolaryngology, carried out the examinations. Numerous conferences were held with the exam-

ining otolaryngologist to clarify the objectives and techniques of the study. A check list was prepared on which only observable physical signs were recorded, with no attempt made to relate these findings to diagnostic categories. The examiner was not informed of the postmedical history or hearing levels before or after the examination.

The definition of an otoscopically abnormal ear, as used in this presentation, is an ear which, at the time of examination by one of the study otolaryngologists at the school test site, exhibited any one (or a combination) of the following physical signs:

a. Congenital malformation of the pinna, auditory canal, or tympanic membrane;

b. Operative scar, adenopathy or fistula in the auricular region;

c. Abnormal coloration, increased vascularization, bulging, retraction, scarring, impaired mobility or perforation of the tympanic membrane;

d. Calcium plaques on the tympanic membrane;

e. Discharge from the middle ear;

f. Cholesteatoma; or,

g. Tumor of the middle ear.

The mean and median values of pure tone air conduction hearing levels of otoscopically normal children in this study are shown in Figure 1. These values were taken from untrained but co-operative listeners, evenly distributed in age between 5 and 14 years, attending school, and functioning without apparent illness.

The mean hearing levels of otoscopically normal children, expressed in sound pressure levels re 0.0002 dyne per cm^2, are compared as a group with the present American standard in Figure 2.

The percentiles of hearing level distributions of this group is shown in Figure 3. This broad distribution is due in part to the difference in hearing sensitivity at the different age levels. This difference is shown for selected frequencies in Figure 4.

Of the children with otoscopic abnormalities, approximately one-third had both ears involved, the remainder only one ear. The

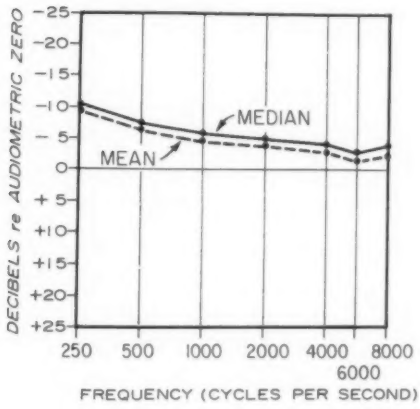

Fig. 1.—Mean and median hearing levels in 2891 otoscopically normal children (re audiometric zero).

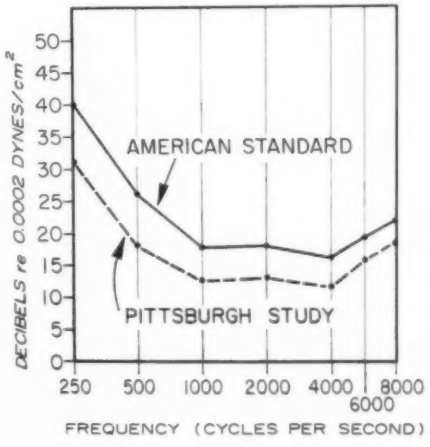

Fig. 2.—Present American Standard (705A earphone) and mean hearing levels - Pittsburgh study (2891 otoscopically normal children 5 to 14 years).

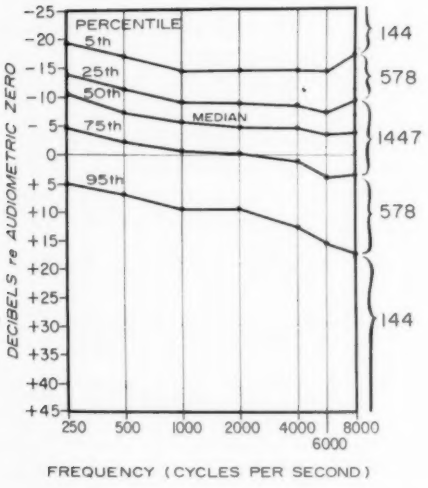

Fig. 3.—Percentiles of the hearing level distributions of 2891 otoscopically normal children (right ears).

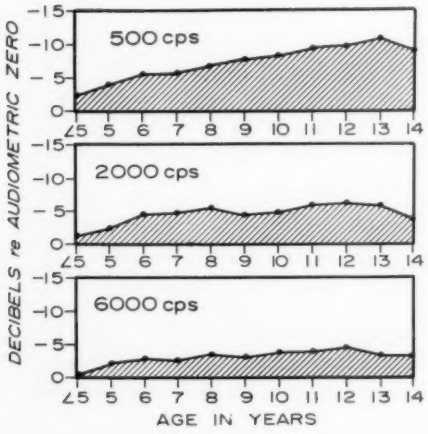

Fig. 4.—Otoscopically normal ears, median hearing levels by age, selected frequencies.

number of ears reported by the otolaryngologists to show various physical signs relative to the tympanic membrane are listed below, with each ear appearing in one classification only:

1.	All perforations, with or without discharge	41
2.	Increased vascularization (only sign)	58
3.	Fullness or bulging, with or without lack of lustre and transparency	11
4.	Discoloration, plus impaired mobility, plus retraction of pars tensa	82
5.	Retraction of pars tensa, plus other signs than those in 4.	134
6.	Retraction of pars tensa (only sign)	108
7.	Retraction of pars flaccida (only sign)	71
8.	Impaired mobility (only sign)	84
9.	Scarring (only sign)	173
10.	Calcium plaques (only sign)	62
	Total Ears	824

Percentiles of the hearing level distribution of the otoscopically abnormal children are shown in Figure 5. Hearing levels show a wider range, and generally less sensitive hearing, than the otoscopically normal group.

For purposes of illustration in this presentation, two groups were selected for further analysis: one with dry perforations of the tympanic membrane; and the other a combination of signs suggesting serous otitis media.

The mean hearing level for ears with dry perforation is shown in Figure 6. Thirty such ears were reported, having a range of hearing levels, from minus 18 db to plus 48 db.

The mean hearing levels for 82 ears which showed a combination of signs suggesting serous otitis media is shown in Figure 7. These ears had hearing levels ranging from minus 21 db to plus 39 db.

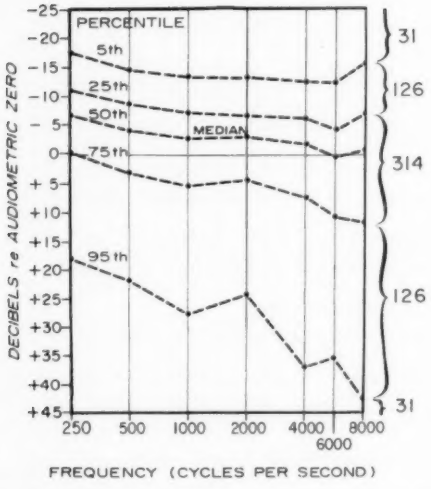

Fig. 5.—Percentiles of the hearing level distributions of 629 otoscopically abnormal children (right ears).

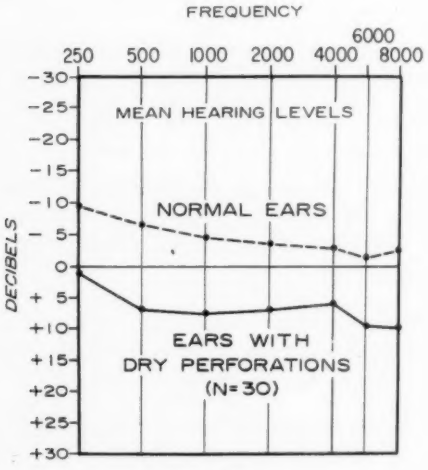

Figure 6

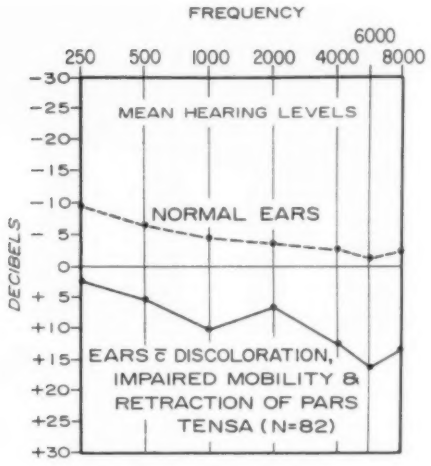

Figure 7

It is obvious that conventional screening levels will fail to identify many of these conditions. For example, in Figure 8 we show the percentage of ears with dry perforations which had hearing levels more sensitive than plus 20, 15, 10 and 5 db. Sixty per cent of ears with dry perforations would not be identified if screened at plus 20 db. Even at plus 5 db, 40 per cent would be missed. In Figure 9, we present similar information for ears with serous otitis media, showing that 85 per cent would be missed at plus 20 db, and approximately 50 per cent at plus 5 db.

It has been assumed in the past that conventional audiometric screening would reveal not only those children with hearing loss, but also those with ear conditions needing medical care. Our data indicate that audiometric testing, however complete it may be, cannot identify all physical abnormalities of the ear in children which may need medical treatment, or which may have predictive value. We believe these findings suggest a need for re-examination of existing techniques for hearing conservation in children.

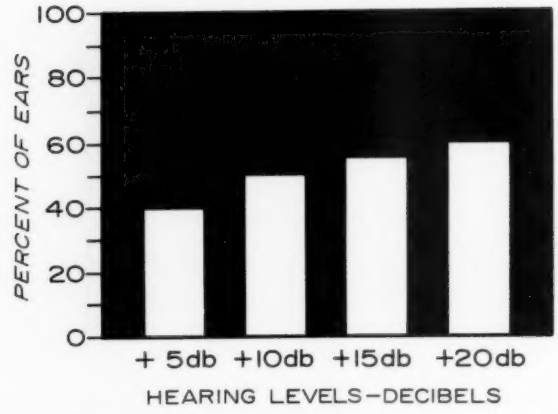

Fig. 8.—Percentages of ears with perforation passing selected screening levels.

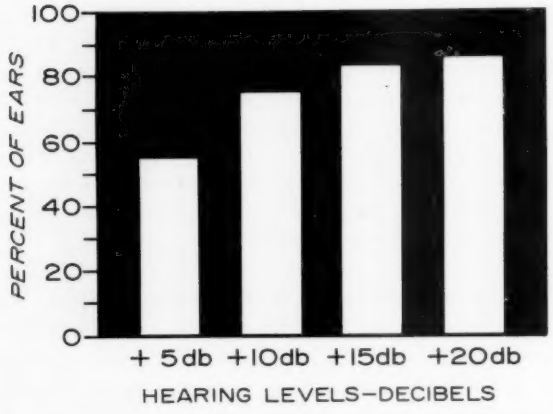

Fig. 9.—Percentages of ears with discoloration, impaired mobility and retraction of pars tensa passing selected screening levels.

SUMMARY

1. The relation of air conduction audiometry and otologic abnormalities was studied in 4067 children—age 5 to 14 years.

2. Acoustic environment and testing techniques were carefully controlled.

3. Precautions to ensure consistency and objectivity of otologic examination are described.

4. Careful audiometry will identify hearing loss, but will not by itself reveal all physical abnormalities of the ear in children which may need medical treatment or have predictive value.

3515 Fifth Ave.

Financial support is provided by grant number B 2375 from the National Institute of Neurological Diseases and Blindness, of the National Institutes of Health; the Children's Bureau, Department of Health, Education and Welfare, through the Commonwealth of Pennsylvania Department of Health to the University of Pittsburgh and the American Academy of Ophthalmology and Otolaryngology.

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LXII

THE FURTHER DESTRUCTION OF PARTIALLY DEAFENED CHILDREN'S HEARING BY THE USE OF POWERFUL HEARING AIDS

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At the beginning, it is thought best to point out that this report is based on clinical otological observations and not on laboratory experiments. Although the use of binaural hearing aids in certain types of cases will be condemned, this report is not intended to

a) Question the fact that for the recognition and interpretation of speech there is both a binaural summation and a binaural integration, or

b) Question the fact that in certain cases the use of binaural amplification is the only answer. The personal experience of an eminent past president of this Society is proof of this last statement.

It would seem that the first published inference of binaural summation was by Seebeck[1] in 1846. In 1943, your present essayist[2] reported that children with a bilateral hearing loss could not hear pure tones binaurally any better than by monaural testing of the better ear but that this same individual could hear and analyze speech much better binaurally than he could in his better ear alone.

Since 1936, it has been the writer's privilege to supervise the Hearing Conservation Program in the Cleveland, Ohio, Public and Parochial Schools. At the present time, these two school systems have a student enrollment of over 200,000. During these years, many changes in procedures have been instituted. In 1938, there was started a procedure which over these years has proven to be the real core of this program. This was the establishment of a central otological diagnostic clinic for all children with a suspected hearing impairment. This clinic is located in our Alexander Graham Bell School

which is the oldest public (supported by school tax funds) school for the education of deaf children in the United States. This school was started in 1893 and has been in continuous operation on the same site ever since then.

At this clinic, we attempt to diagnose the presence or absence of a hearing loss in these referred children. Of those positive cases, we try to establish the degree of loss, its potential remediability, its etiology and then make appropriate recommendations. This is accomplished by 1) having at least one parent present; 2) obtaining a complete otological history including the dates and severity of all prior illnesses; 3) making a complete ear, nose and throat examination; and 4) making a pure tone threshold audiometric test. When necessary in order to confirm or make an etiological diagnosis some of these children are subjected to bone conduction audiometry and speech audiometry or both.

Since 1938, we have records on more than 8800 children. Of this number about 2000 have had more than one test and about 800 have had at least four tests. In 1953, Dr. H. L. Williams asked me to report before a Triological Society meeting an analysis of this rather large series of hearing tests on these children. In this report[3] it was stated in referring to 16 cases of progressive sensori-neural hearing loss that "the progress was not noted until a wearable hearing aid had been put on these children and in every instance the increased loss was more marked in the ear in which the hearing aid was used." From 1953 to the present time many writers with international reputations have reported on noise induced hearing loss in some industrial workers whose hearing had been normal before exposure to sustained high noise levels. The fact that this can happen is disputed by no one although some of the important problems are still unsolved. One of these problems is the matter of "susceptibility." During the years from 1953 to 1956, your essayist had many personal discussions with experts in the field of acoustic trauma. In these discussions, the question of hearing aid trauma was brought up and every time this possibility was deprecated. It was only natural to assume that my 1953 observations had been in error and for several years it was forgotten. Last year a rather exhaustive search of the American literature on this subject was made. It was found that in 1957, Silverman[4] stated, "The evidence from the relations of hearing loss to noise exposure suggests the possibility of damage to an ear exposed to the

level of sound pressure generated by a hearing aid." Maybe other American writers have mentioned this possibility but none was found.

From the years of about 1955 to 1959, American hearing aid manufacturers were vying with one another to produce hearing aids that were smaller, more disguisable, more powerful and with greater fidelity. Now one prominent manufacturer claims that they produce a small aid with five transistors and two transformers which has a fidelity range of up to 4200 cycles with a maximum acoustic gain of 80 decibels and a power output of up to 146 decibels. This writer questions the last of these three claims but the fact that most of these aids are now very powerful is without question.

About two years ago, there was started the idea of fitting children of between the ages of two and twelve years with binaural hearing aids[5] of one of these powerful makes. An ear piece was molded to fit each ear and a metal spring bar went over the top of the head to hold these two earpieces tightly in the ear canals. A hearing aid microphone and amplifier was attached to each side of this metal headpiece in order that this small aid would be just superior to and behind the upper part of each auricle. It is presumed that such an arrangement was devised in order to make it more likely to stay in place and also to decrease the likelihood of feedback. We have observed that it fulfills the latter point, even when such powerful aids are turned up to maximum capacity. It would be most interesting to try to ascertain if the sound pressure within an ear canal of a subject wearing an aid by this method is increased over the maximum pressure in the same ear canal when the aid is worn in the more conventional manner. It is logical to assume that this method itself might increase the ear canal sound pressure. As far as can be ascertained this investigation has never been done. At no place can one find that the development of this kind of amplification was done under otological supervision or approval. It is claimed by the proponents of such hearing aid fittings that "speech intelligibility can be increased by fourfold." This has never been proven on the basis of speech audiometry by use of spondee words and it is impossible of attainment from a neurophysiological viewpoint.

Keys,[6] Hirsh,[7] Bocca[8] and Bergman[9] have reported on the probable advantages of binaural hearing aid amplification over monaural amplification. In none of these reports is there anything like the four

times better results previously mentioned. As a matter of fact, the inferences in some of these reports are not borne out by their own figures. On the other hand, Dicarlo and Brown[10] found that binaural amplification actually reduced the speech reception threshold in their series of cases.

In consideration of the education of the totally or subtotally deafened child one can find no fault with the use of binaural amplification of even very high intensity. It is a matter of nothing to lose and the possibility of some gain.

During the past two years, we have been privileged to make some repeat hearing tests on partially deafened children who had been wearing these powerful hearing aids of both the monaural and binaural type. This stimulated me to start another study to see if there may not have been some merit in the observations first reported in 1953. In October 1960, a communication was received from Dr. Rejakjar,[11] Director of the Hearing Rehabilitation Center in Odense, Denmark. In this paper, he confirmed my observations of 1953. He also refers to papers of Gromov[12] and Dunajvitser[13] who have been making similar observations in Russia. This lent stimulus to my project and herewith is reported my findings.

The files on every one of the previously mentioned 8800 children were examined individually.

The following criteria were used in selecting certain records for further study:

1) The child must have been wearing a hearing aid for at least one year.

2) There must have been at least one pure tone threshold hearing test on this child prior to the use of the hearing aid.

3) There must have been at least two similar tests after six months' use of the aid.

4) The diagnosis of the etiology of the hearing loss must have been fundamentally of a sensori-neural type.

(To otologists it is not necessary to stipulate the points in making such a diagnosis but to others it may be well to so stipulate.)

a) There was no history of purulent discharge from either ear.

b) Visual examination of the eardrums showed that both were normal.

c) There was no clinical or visual evidence of obstruction in the nasopharynx.

d) Approximately 38% of the selected records showed that bone conduction testing had been done and this testing confirmed the diagnosis as one of perception loss.

e) Approximately 10% of the selected records showed that speech testing had been done and the discriminaiton score confirmed the diagnosis.

5) Each record must show that the child had normal or nearly normal speech. *Therefore the development of speech in these children was of no importance.*

Criterion 2 meant that 6 years of age was the minimum age of the first examination of these selected records. Actually 16 years of age was the oldest of any of these cases. Approximately half were boys and half girls. Because of these criteria seven of the 16 cases referred to in the 1953 report have not been included in this report.

Because of the desirability of having some sort of control in this study, these records were divided into two groups. The first group which I choose to call my control group were those children who had been studied according to the mentioned criteria from 1938 through 1958. During these years, the aids used were less powerful and always used monaurally. Of the 178 selected cases, 146 were in this control group. The remaining 52 cases that had been selected according to the previously mentioned criteria were cases that had been studied during 1959 and 1960.

Of the 126 cases in the control group, 5 showed an increased loss of an average of 10 db in the speech range in the used ear. Eight showed an increased loss of an average of 20 db in the used ear. This means that 10.3% of these 126 showed a further loss of hearing in

the ear in which the aid had been used. Four cases (3.2% of the total) showed an appreciable loss in the ear which had not been used but in all four of these cases the loss was more pronounced in the used ear. One hundred nine cases (86.5% of the total) showed no change in their hearing level.

Of the 52 cases in the latter group, 39 used their aid in one ear only. Of these 39, 19 (48.8%) showed an increased loss of an average of 20 db in the used ear. Only 1 of these 19 showed an increased loss in both ears and in this case the loss was more pronounced in the used ear. In this latter group of 52, 13 had been using a binaural aid as described previously. Of these 13 cases, 9 (69.2%) showed an average increased loss of 25 db in both ears.

CRITICAL ANALYSIS

You will note that the use of the word "permanent" has been avoided in considering these increased losses. No one can rightfully talk about these cases as having had a permanent increased loss any more than one should talk about permanent increased hearing after any of the operations performed with such an object in mind. However, it should be pointed out that in criterion 3 in the selection of these records there must have been at least two hearing tests following the use of the aid for six months. In no case did the second or further tests show improved hearing. The averages used were the averages of the last test in each case.

One could logically ask "In how many of these cases would there have been an increased loss if a hearing aid had not been used?" The answer to that question is not easy. During these 23 years and in this series of over 8800 cases the number of partially sensori-neural deafened children with an average loss of 40 db or more in his better ear who have not used a hearing aid was insignificant.

Because the same examiner examined all of these 178 selected cases and by using the same general methods it is felt that division of the control group from the other group is perfectly fair. The only difference between these two groups of 126 and 52 was the power output of the aids being used. It would have been very helpful to have had records as to the hours per week that these aids were worn and to what intensity they were turned to. This was not recorded. How-

ever, it is honestly felt that with respect to these two variables there was no significant difference between the earlier and the latter group.

A start has been made to try to study these 178 cases from an etiological viewpoint. This will take a tremendous amount of mathematical evaluation on a basis of probabilities and possibilities (so-called chi-squaring). As otologists, you will realize that the etiological diagnosis of such cases is presumptive in the majority of instances. In those cases, in which such a diagnosis was made, they were classified as hereditary, post-meningitic, measles virus, mumps virus, erythroblastosis fetalis, toxicity of mothers during the second and third month pregnancy, birth anoxemia and cerebral palsy. It is my opinion that of these etiological diagnoses, the one case that is least likely to have hearing aid trauma is the hereditary case.

My personal feelings as a result of this study are:

1. In sensori-neural partially-deafened children, no hearing aid of more than 40 db gain should be used in spite of the fact that a more powerful aid may possibly give better speech hearing (spondee score) improvement at the first fitting.

2. The use of binaural amplification in such children should be condemned.

3. Children between the ages of five and 16 years who wear a hearing aid should have their hearing evaluated by an otologist at least every six months.

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LXIII

PLACEBOS, ANTI-SLUDGING DRUGS AND DISORDERS OF THE EAR

EDMUND PRINCE FOWLER, M.D.

NEW YORK, N. Y.

I have chosen my title in the hope that it will for a few moments at least attract your attention to certain problems in clinical otology, to the relationship of disorders of the ear to general medicine. Unless we relieve otology from narrow interpretations we will inevitably confine it merely to the techniques in the limited surgical field at its disposal.

First, a few words about the much underestimated, abused, or neglected placebo.

It has been thought that because placebos are "inert" agents and can function only by influencing mental (psychological) states, that making use of them smacks of quackery or unethical practice. This attitude ignores the facts of life. The placebo should not be despised, because when situations occur in which mental reactions influence the picture (as they usually do) the placebo has a good chance of producing a more favorable reaction than would have been possible without it. Certain observations and experiments by Dr. Henry K. Beecher[1] seem to confirm this belief. He reports that, "the mean percentage effectiveness of placebos in relieving pathological pain is over ten times that found with experimental pains." In other words, the effectiveness of placebos increases with increased concern or mental stress, also the effectiveness of certain active drugs increases with increasing concern or stress. He quotes several authors[2] who have "demonstrated that the firing of the adrenal glands (measured in objective terms) is far greater in response to a placebo in patients hospitalized for severe anxiety than in patients hospitalized for lesser degrees of anxiety."

I have used the term "anti-sludging" instead of "de-sludging" because I have never observed a complete disappearance of the sludge.

Over 15 groups of investigators reported comparable results using an active drug (morphine), which in even large doses did not dependently relieve experimental pain but in comparable or even smaller doses was highly dependable, highly effective in relieving pathological pain.*

Anxiety, fear, stress and strain provide the basis upon which the degree of efficacy of the drug (in this instance, morphine) is in part at least dependent. It may be concluded that anything a physician or a surgeon does for his patient includes some placebo effect, and in fact that anything that diminishes or relieves anxiety operates similarly. Without the placebo effect most physicians, and especially the psychotherapists, not to mention all of the chiropractors, would be *hors de combat*.

It may be said that if you do not obtain some placebo effect from a drug or medicine or surgical procedure you had better change your doctor or your disposition, or both.

It would then seem that the effectiveness of treatment in considerable measure is related to the significance of the symptoms, to the amount of anxiety, fear or tension they engender and to the degree of trust in the doctor. The mere fact that something is being done about it tends to diminish pain and the apprehension which it occasions. When we go to our dentist for a toothache the ache may have markedly lessened and sometimes even disappeared before he has looked at our teeth, and consequently we may even have been uncertain as to which tooth had been aching. This is a welcomed effect unless he pulls out the wrong tooth, which has happened.

On the reverse side of the coin, placebos have been known to cause all of the toxic symptoms associated with powerful drugs. Attention has been called to the placebo effect because I believe it is a very real and powerful factor in the successful employment of all drugs.

INTRAVASCULAR PHENOMENA

Since first reading Knisely's paper[3] on sludging some 15 years ago I have been convinced that sludging is a phenomenon observable

* *Definition*: A pathological pain is an autonomic impression upon the sensory nerves causing distress or even severe agony.

in all infectious diseases and in all trauma to the soma or the psyche. I have from time to time discussed this phenomenon and the concomitant autonomic neural (emotional) factors involved and the effect upon metabolism, also its importance in aging and particularly certain types of presbyacusis, neural deafness, sudden deafness (especially from mumps), limited lesions of the basilar membrane, tinnitus, vertigo, and otosclerosis. I have endeavored to incite your curiosity as to the pathophysiology and symptomatology associated with sludging, and faulty metabolism in the auditory apparatus. From the first I have employed the standard slit light head-rest because this device enables one to consume only two or three minutes in examining the blood flow in the vessels of the ocular conjunctiva with the magnification and powerful illumination used by Knisely and Block. My son, Edmund, Jr., seems to be the only otologist who is sufficiently impressed to have initiated research in these matters. His findings tend to confirm the opinions set forth. But an opinion, a point of view, or a philosophy, must be put into practice before it can be fully substantiated. Herein I shall briefly discuss the basis for my philosophy and some of the results observed by putting it into practice.

Until recently almost all of the data we possess concerning the blood has been obtained outside of the vessels (in "vitro" or out of "vitro") and therefore our knowledge of intravascular blood physiology and pathophysiology has been hypothetical, confused and questionable—verily a tangle of unsolved problems. Blood smears do not reveal sludging, nor does the cell count, hemoglobin percent, hematocrit data, sedimentation rate or prothrombin level closely correlate with the severity of sludging.

Sufficient intravascular agglutination ("sludging" or "clumping") of the blood would seem capable of contributing to many of the symptoms in many diseases and engendering all of the initial symptoms of true fibrous embolii. But unlike localized fibrous embolic lesions sludge is usually distributed throughout the blood stream and the agglutinates generally continue to move through the bottlenecks. It may be that some sludging is always present, and that when detectable it is only an exaggeration of a normal phenomenon. It may be that it is a precursor but not necessarily an inciter of clotting. It may merely set the stage for it. At any rate clotting does not appear to occur until there is a preliminary agglutination or sticking together of the cells of the blood, and sludging certainly is just this. The

great mystery is why the cells do not always stick together, and why when some do, as in sludging, all do not stick together.

Like all protein bodies the blood cells are sticky and so is the fluid in which they are maintained, the plasma. Is it because the rate of flow, the turbulence, or Brownian movements sufficiently disturb the plasma to tumble the cells along in the blood stream with sufficient agitation to prevent their sticking together? It would not seem so because if you look at a slow motion magnified picture of blood flow it is evident that in health even in very slow moving venous blood the cells seem to readily pass by each other and along the vessel without sticking either to them or to each other.

In the small arterioles, the precapillary sphincters, and the venules and especially in the capillaries themselves some amount of stasis always obtains because of the crowding and slowing incident to passage through these bottlenecks. When physiological this slowing down is beneficial because it facilitates the transfer of metabolites, and particularly of oxygen to the tissues, and the cells then do not stick together. If severe it is pathophysiological and then it does cut down the availability of the oxygen, minerals, and other metabolites in the blood, and the cells then do stick together.

It is interesting to learn from Hemmingsen and Scholander[4] that "the transport of oxygen through Hb. solutions is abolished when opposed by even a slight back pressure of oxygen." Surely there is a back pressure of oxygen when stasis and sludging occur and not only in the hemoglobin solution in the plasma but also in the hemoglobin solution within the intact red cells. Hemoglobin constitutes three-quarters of the solid content of the cells.

ELECTRICAL POTENTIALS

Electrical potentials are present in all living cells. The air we breathe is loaded with potentials. There is good evidence that potentials originate biochemically in all ganglion cells, and of course in some of the neural end organs where they result from stress whether it be a piazo-electric twisting, shearing stress, or a more linear stress with a more simple mode of production. It is hypothesized that acetylcholene and cholensesterase play a major role. Other enzymes would

also be involved. The subject of potentials in normal blood cells deserves more investigation by experimental physiologists.

However, no matter by what means potentials are generated if the blood cells are to be kept apart by electrical potentials their charges must be the same (either plus or minus) because otherwise the cells would not repel but would attract one another.

Whether the blood is considered to be a suspension, an emulsion or a colloidal solution, or a combination of these states, it is logical to believe that the cellular elements are kept apart by potentials.

It is the cell membrane "which is the site of the electrostatic and chemical forces which give rise to the potential difference between the inside and the outside of the cell."[5]

The cell potentials are maintained by the insulator membrane which consists largely of lecithin, cholesterol and nucleo protein. This means that we can think of the cells as tiny condensors each probably having a potential of about one micro volt. Even larger potentials have been found in other living cells.

Trauma, anoxia and oxidative poisons dissipate potentials and would therefore tend to dissipate the forces keeping the cells apart. Potentials are dissipated instantaneously. Please note that almost instantaneous is the appearance of sludging in the blood.

Excessive squeezing of the films covering the one or two molecule thick red cell membrane could bruise and therefore destroy its insulating power and nullify at once the surface potentials necessary to keep the cells apart, and they would then stick together and remain stuck unless forced apart by intermittent contractions of the arteriolo-capillary sphincters and made less adhesive by anti-sticking substances in the plasma or both. Heparin® and Dicumeral® and such-like drugs diminish stickiness, they lower plasma cholesterol (as nicotinic acid is said to do), they are anti-lipemic.

It is important to realize that even when only 10 red blood cells stack together 90% of their surfaces are smothered and oxygen availability from them is cut down markedly; also that the transport of oxygen by the blood plasma is always less than by the red blood cells.[6]

The red blood cells are readily affected by alterations in the plasma in which they are contained, if hypotonic it swells them, even bursts them producing ghost cells. If hypertonic it shrinks them producing stellate and crenated shapes.

The biconcave structure of the red blood cells suggests that they would be subject to a cupping effect (a partial vacuum), especially when they are squeezed and stacked into rouleau in the arterioles and this may be a factor in the clumping process. Of interest is the tendency of each of the three types of blood cells to segregate and largely exclude the others in the masses. And so we have a few facts and a few notions to explore in our search for the truth.

Many things affect blood lipids and therefore sludging. A hearty meal increases them and Heparin diminishes them by stimulating the enzyme "lipoproteid lipase." Heat (and therefore fever and electric shock) increases their fluidity. High fevers can markedly increase the fluidity and diminish the thickness of the lipid insulation films surrounding the red blood cells and render them more easily traumatizable and liable to the loss of any potential they may have possessed. The cells would then be more likely to stick together and form sludge. However some of these factors might lessen stickiness. The point at which, or why, one or the other of these opposing forces would predominate is not known.

EFFECTS OF SLUDGING

It is not the mere presence of clumping that causes trouble; probably over 90 per cent of the people in this room have some sludging of their blood, especially if they violently disagree with me. It is the size and consistency of the masses and also the spacing and the rate of blood flow that is important. Except in extremis the larger the masses the larger the spaces between the masses, the slower the flow, and the fewer the cells between the masses. Why this does not produce an increased hemopoiesis we do not know. The location and amount of impedance encountered by the masses in the smaller vessels, and the time factor, determine the degree of asphyxia from the anoxia, local hypometabolism, and lowered health in the tissues affected.

Did you ever wonder why the outer hair cells of Corti's organ are so often found to be affected alone or before the inner hair cells?

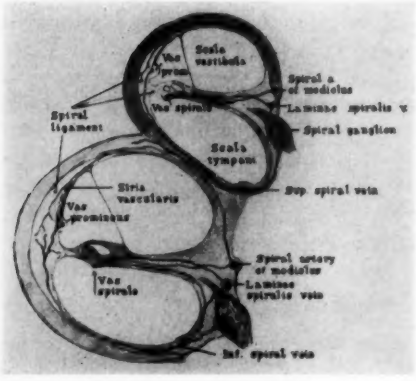

Fig. 1.—Diagram of a section of the 1st and 2nd turns of the cochlea showing the main blood vessels. Adapted from Anson and Bast, "The Temporal Bone and the Ear."

Have you wondered why the higher frequencies are more affected in presbyacusis, in certain toxic poisonings and acoustic shock? Of course, you have!

If the nutrition of Corti's organ and supporting structures is not wholly by way of the endolymph, as would seem probable, then it could be furnished also by the terminals of the vessels in the spiral ligament (the basilar membrane) which are visible in the basilar membrane beneath Corti's organ and therefore are in a position to furnish some nourishment to this structure.

At all levels the bony spiral lamina is progressively narrower as it ascends toward the apex and its blood vessels are longer and proximally larger in the lower than in the upper turns. This makes the supporting structures of the outer hair cells more distant from the blood supply from the spiral artery in the modiolus than the supporting structures of the inner hair cells. The vessels to the stria vascularis, and to the spiral ligament via the bony spiral partition are 2 or 3 times as long as the vessels to the area below the inner cells of Corti's organ. To reach the basilar membrane supporting the outer hair cells

of Corti's organ in the basal turn the blood by either of these routes has to travel a greater distance than to reach the basilar membrane supporting the inner hair cells of Corti's organ. This, under some circumstances, would tend to render the larger longer vessels liable to plugging by sludge before the smaller, shorter vessels to the inner cells beneath Corti's organ; also to the shorter vessels in the upper turns. Large masses might even bypass and be excluded from the shorter smaller vessels and pile up only or more in the larger and longer vessels. Such bypassing phenomena have been observed.

Of special interest to the otologist is the thought that if the oxygen supply from the hemoglobin in the red blood cells is cut down not only is the major supply by way of the stria and the endolymph diminished but also the supply direct to the base of Corti's organ. Also that the oxygen in the endolymph is derived from the blood and sludging will diminish the supply of oxygen and other metabolites via this source. However, since the area below the inner hair cells is nearer to the direct blood supply and therefore probably less dependent upon the endolymph, this area and its supporting and superimposed hair cells might still receive sufficient oxygen to survive when the more distant areas would succumb to an anoxia caused by vascular agglutination and even to other causes of asphyxia. Clinical experience fits in nicely with these observations. Of course I am here referring especially to an anoxia caused by slowly moving masses of sludge, not to immobile emboli.

For years we have wondered how in otherwise apparently healthful people a narrow gap may develop in the threshold audiogram curve. The unavoidable answer would seem to be that the circulation in the membranous labyrinth being terminal any local damage by trauma to the organ or any prolonged impedance to the blood flow to the base of Corti's organ will partially or totally put out of business only the local area affected. However, a local lesion in the stria vascularis at any level will affect not only the whole of the endolymph in the scala media but eventually will affect that in the saccule and utricle and semicircular canals. Likewise a local lesion involving the tunnel of Corti will affect the whole of its fluid. The amount of trauma and anoxia will determine the functioning level of the tissues affected. If the anoxia is long continued there will be no reversal. At present no other answer seems as plausible as the one given. However, if anyone thinks he has one let him speak up so we may discuss it.

Keep in mind that the vessels in the stria vascularis invariably contain the sludging blood and it therefore does not seem too far fetched to believe that sludging phenomena can engender endolymphatic hydrops and some or even all of the symptoms associated with it. Simply stated, hydrops is an increase in fluid, an edema, and sufficient sludge causes edema. Someone will say you cannot have it both ways. How is it that in hydrops it is the lower frequencies that are affected whereas in neural hearing loss without apparent hydrops the higher frequencies are usually the ones more or alone affected? One answer is suggested, namely that although the hydrops exerts pressure equally in all directions it will distort the more movable regions of the basilar membrane more than the less movable regions. In other words, it will distort the broader, more displaceable upper regions more than the narrow less displaceable basal regions of the basilar membrane and thus favor a loss of function in the upper turn, not necessarily in the lower turn unless sufficient sludging occurs to affect all turns. It may be that vascular impedance as well as the increased pressure from the hydrops operates to cause the anoxia in Corti's organ.

ANTI-SLUDGING DRUGS

Many drugs have been used to lessen sludging. Some may be thought of as de-sticking drugs. A few of the more commonly employed are, in addition to the anti-clotting, anti-lipemic, hemorrhaging drugs such as Heparin and Dicumarol (which diminish adhesiveness, and diminished cholesterol in the plasma), those drugs that do not cause bleeding, namely the salicylates (particularly aspirin), chlorophyl (Derifil), nicotinic acid, quinine and more recently the antimalarial quinine related drugs such as hydroxychloroquine sulfate (Plaquenil), all of which have been employed by others to combat intravascular clotting.[7] But sludging is not a fibrous clotting and fibrolytic enzymes would seem not to be indicated, and they are dangerous and limited in time. We have experimented with most of these drugs as well as observing the effects of nitroglycerin and procaine preparations. Immediate transitory as well as some prolonged changes in the sludging of the blood following their use have been observed, but it must be said also in a few instances in the absence of their use.

All patients suffering from Ménière's disease or tinnitus who improved without the antisludging drugs did not receive them. Only

the 24 here reported who did receive the drugs experienced sufficient improvement to warrant prolonged treatment. With intermissions five patients have continued treatment for three years.

Because of the small number of patients treated our results with the antisludging drugs at this time deserve but brief attention. The following abstracts and summary will suffice.

ABSTRACTS OF HISTORIES

Of the twelve patients taking chlorophyl only four had binaural progressive deafness.

1. Male, now 16 years of age, severe loss of hearing 6 years ago; hearing in right ear stabilized, in left ear improved some; no tinnitus.

2. Male, now 46 years of age; after four months tinnitius and deafness in right ear much less and also his allergy.

3. Male, now 71 years of age; in one week tinnitus and deafness diminished in both ears, using hearing aid now only on special occasions although audiometric tests show little change in hearing.

4. Female, now 33 years of age; hearing unchanged after four months but tinnitus now seldom noticed.

Three had monaural total deafness.

5. Female, now 68 years of age; derived no benefit in hearing but is much better stabilized emotionally.

6. Male, now 33 years of age; Ménière's disease; no attacks since he has taken the medicine unless he omitted it for a few days; resumption immediately stopped his vertigo; health markedly improved.

7. Female, now 44 years of age; monaural otosclerosis (twin sister has binaural otosclerosis). No change in hearing but no tinnitus now.

Three had presbyacusis.

8. Male, now 76 years of age.

9. Female, now 69 years of age.
In both tinnitus was distinctly less and the general health improved including the allergy suffered by the female.

10. Female, now 71 years of age; no change in hearing after two months of treatment but improvement in health and emotional stability and the tinnitus was much less annoying.

One had sudden total deafness in left ear and almost total in right ear.

11. Male, now 40 years of age; specific history in family but all Wassermann tests negative for years; marked recovery in hearing in right ear; resumed regular classes in school. Hearing has improved 5 to 10 db in all of the frequencies from 250 to 4000. Sludge distinctly less.

One had bilateral deafness and tinnitus.

12. Female, now 64 years of age; developed rhetinitus pigmentosa at 50 years of age; tinnitus in both ears. Had acute otitis media which cleared up and the hearing improved markedly and the tinnitus lessened in both ears.

One patient received both Dicumarol and Chlorophyl.

1. Male, now 61 years of age, suffered from a slowly progressing binaural deafness for 15 years when left ear suddenly became totally deaf with loud binaural tinnitus for many months and roaring in one ear. Sludge marked. Specific history 35 years ago, negative since. Dicumarol produced a marked diminution in tinnitus and in sludging and he could again hear his own voice. Had some right upper teeth pulled and nearly died from hemorrhage — several transfusions. Switched to chlorophyl. Sludge diminished and the tinnitus did not bother him until an automobile accident when sludging and tinnitus increased. Tinnitus now sometimes disappears and the sludging is less. No dizziness for months. Wears a hearing aid.

Four patients first took chlorophyl and subsequently plaquenil. All sufferred from binaural progressive neural deafness.

1. Female, now 60 years of age; had loud tinnitus. The sludge markedly diminished after 8 months with some intermission and her tinnitus disappeared but later returned in her poorer ear. Switched to plaquenil which markedly lessened the sludge and again the tinnitus disappeared. Also has had no intermittent claudication since taking these medicines.

2. Male, now 74 years of age; took medicines but with long lapses in treatment. No marked change in hearing until recently when the hearing improved from 5 to 10 db in the right ear and 5 to 10 db in the left ear with a marked improvement in appearance and in health. No longer needs hearing aid except on special occasions. In the middle of April 1961 a further 5 to 10 db improvement in hearing in the lower tones and in one ear in the mid tones.

3. Male, now 67 years of age; took large amounts of quinine in youth and subsequently many drugs for various complaints including diabetes. Sludge marked. Chlorophyl started three years ago and in a little over a month the circulation was improved so that the tingling in his fingers was better and pain less and there was no further intermittent claudication. Also took aspirin four times a day when pain was severe. Sludge finer and better flow. Began plaquenil in 1960 with aspirin PRN. In one week noticed improvement and in his general appearance. Has not felt so comfortable for ten years. When he omitted the medication for three or four weeks exacerbation of symptoms occurred with marked increase in the sludging but not in as long strings as originally and the hearing diminished 5 to 10 db in the mid frequencies. Now no tinnitus or cramps and is improved in health.

4. Male, now 40 years of age; binaural excessively loud tinnitus. No improvement in hearing or in tinnitus until March 1961. Had switched to plaquenil six months previously. Now his right ear, formerly down 30 to 40 db in the speech frequencies, has improved to average normal at 1000, 5 db at 2000 and 10 db at 4000. Bone conduction also improved to no loss at 1000 and with but little change in the frequencies above and below this. The opposite better hearing ear also improved at all frequencies so it is now down only 5 to 10 db. Tinnitus is better tolerated. Patient improved emotionally.

Six patients took plaquenil only; two had binaural neural deafness above 2000.

1. Female, now 56 years of age; the tinnitus improved and is now in only one ear. The health is much improved and the sludge is less marked.

2. Male, now 36 years of age; much improved in general health, tinnitus no longer bothers him.

One had binaural progressive neural deafness and binaural tinnitus.

3. Male, now 64 years of age; no improvement in hearing but binaural hearing aids help greatly. Plaquenil for five months intermittently; less disturbed emotionally, more stable and tinnitus is less.

MÉNIÈRE'S DISEASE

4. Female, now 70 years of age; plaquenil intermittently for 11 months. After two months muscular tremor diminished and Ménière's symptoms disappeared except for a few times during intermission of medicine when they followed emotional upsets but no real vertigo since taking plaquenil, and no intermittent claudication.

One had total deafness in one ear, presbyacusis in opposite ear.

5. Male, now 71 years of age; chronic profuse rhinorrhea, cause unknown, also Paget's and Parkinson's disease. During pneumonia in 1960 rhinorrhea ceased but returned on recovery. Plaquenil lessened his leg cramps.

One had binaural total deafness and binaural tinnitus.

6. Male, now 55 years of age; first examined 25 years ago when hearing was lowered 50 to 70 db in speech area in both ears. Six years ago total deafness in both ears and severe attacks of non-directional vertigo following emotional upset. BMR-18. Tinnitus severe. No improvement in hearing but hearing aid is of some value. Tinnitus usually no longer annoying.

SUMMARY

I have discussed the placebo effect inherent in all treatment; I have set forth some facts and notions concerning the intravascular agglutination of the blood and its possible role in the causation of hypometabolism and its role in certain diseases and disorders of the ear. I have briefly reported my results with some antisludging drugs.

It should be noted that most of these patients in addition to an improvement in hearing and a lessening of tinnitus also improved in general health as well as in relief from a variety of other symptoms. There were no undesirable side effects. For what it may be worth although most were older people none have suffered a coronary.

I am in grave doubt whether the observed improvement in symptoms was in a given instance due wholly to the drug used, or also in part or wholly to the placebo effect inherent in all treatment (even with self-administered treatment, with aspirin and the vitamins). Remember, for generations our fathers usually included quinine in their tonics and it certainly was often beneficial to the patient. But this went out of fashion until recently when we have swung full cycle and again are using the anti-malarial quinine drugs.

Were the old tonics more beneficial because of their antisludging or their placebo effect?

Even though results be meager or uncertain you must persist in searching for the truth, you must never cease to explore, to maintain your verve and joy in investigating the unknown or the uncertain. You must never give up.

140 EAST 54TH ST.

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LXIV

HEREDITARY NERVE DEAFNESS

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AND

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(By Invitation)

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Fourteen years ago interest was aroused in a single kindred showing hereditary nerve deafness. Studies to try and establish the mode of inheritance, and the anatomic location of the lesions have been attempted during this period. It was hoped that this information might give a clue to the physiologic pathology of hereditary nerve disease, and perhaps yield an approach to its treatment. The Mormon community presents a unique opportunity for the study of hereditary disease. Since it is an agrarian population, which does not move from its farms, its members can be relatively easily located. Because of this, a gene may be followed from a single polygamous male through generations of a rapidly expanding population.

Key members of the family were located and interested in the disease. They aroused family interest until members would congregate in selected homes, where histories were taken and physical examinations were performed.[1] These key members would often keep after unwilling members of the family until they would also co-operate in the study. The records of the Genealogical Offices of the Church of Jesus Christ of Latter Day Saints often helped to locate members of the family whenever difficulties were encountered. A complete history was obtained from each individual of that kindred, who could be contacted. If the individual was not living, or not easily available, the questions were asked of close members of his family. These histories were rechecked by the cross-questioning of other family mem-

From the Laboratory for the Study of Hereditary and Metabolic Disorders, and the Departments of Medicine and Surgery of the University of Utah College of Medicine. This study was aided by Grant A-2 from the U. S. Public Health Service.

bers who knew the individual. Unless the records agreed, the data were not used until such time as a coherent picture could be obtained.

At the family gatherings, information was obtained about the age of onset of the disease, its duration, the treatment, if any, and whether there were any intercurrent infections or other pathology. These data were used, both in an effort to understand the development of the familial trait and to properly classify any member whose auditory difficulty was the result of nongenetic causes. Physical examination consisted of inspection of the ear, nose and throat. Various ancillary observations for taste deficiency, A, B, O blood group and eye color, were performed to establish concurrent genetic patterns. However, no linkage relationships could be established. The cervical glands were palpated and the condition of the external ears, canals and drums were noted. Auditory examinations, consisting of spoken and whispered voice tests with masking, the Rinne and Weber fork tests, and finally audiograms, were performed. These were made in a quiet room during the home visits. The examinations were continued by checking the nose for septal deflection, sinusitis, the appearance of the mucous membrane and of its exudates. The teeth and their occlusion were examined to rule out a Costen syndrome.[2] The condition of the mouth, tonsils, tongue, pharynx and larynx was noted. These examinations were repeated at three to five year intervals, so that the developmental aspects of the disease could be studied.

The pattern of inheritance of the trait is fairly clear. It is transmitted in an unbroken line from parent to offspring, is not sex-linked. It shows the expected appearance of the trait in half of the children of the affected parents. See Table I, prepared from analysis of 24 siblings arising from affected individuals in four generations in this kindred. This indicates a simple autosomal dominant trait. This pattern was established by data accumulated about 348 descendants of a single polygamous male (Fig. 1). Eighty-two individuals were found who had impaired hearing in the speech range. Eleven of these were due to varying causes of a nongenetic nature, leaving 71 cases representing the familial type of hearing impairment. There were, in addition, 20 children with high tone loss, which is believed to represent the early stages of this hereditary defect. The trait occurred in one-half of the children, when either parent had the trait, and occurred with equal frequency in males and females. The gene appears to be fully penetrant. No individual possessed the trait

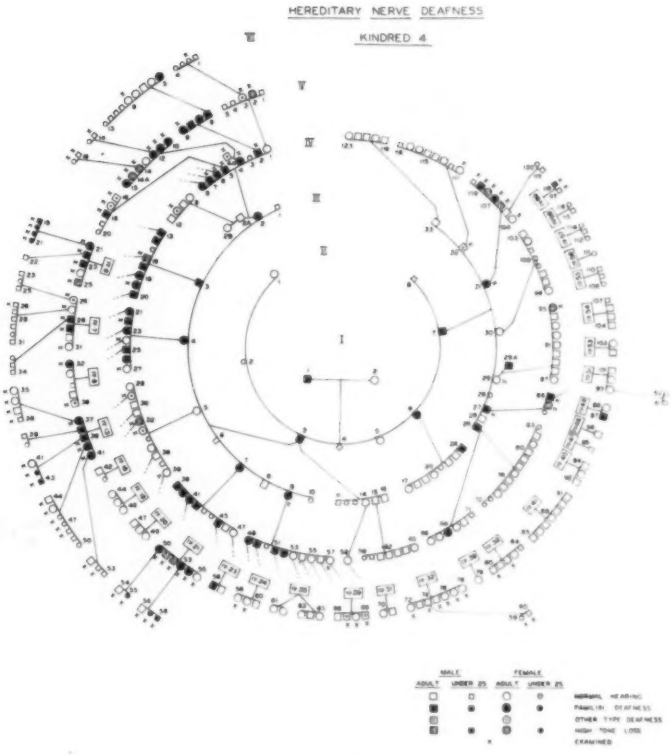

Figure 1

unless a parent was deaf, and half of the children of an involved parent showed evidence of the disorder.

The condition of the tonsils, adenoids, dental occlusion, allergy, septal deflection, sinusitis, and edentulous states did not appear to affect the appearance or progress of the deafness to any degree. Selected patients showing hearing loss were sent to the rehabilitation center of the University of Utah, where the audiologic group carried out speech audiometry, tone decay and recruitment tests. To establish

TABLE 1

CLASSIFICATION IN 24 SELECTED FAMILIES

PARENT	HEREDITARY DEAFNESS		CONDITION OTHER THAN DEAFNESS		HIGH TONE LOSS		NORMAL		CONDITION UNKNOWN	
	M	F	M	F	M	F	M	F	M	F
2 - 3 -	1	4	0	0	0	0	3	2	3	3
2 - 6 -	1	0	0	0	0	0	4	2	1	0
2 - 7 -	2	1	1	0	0	0	2	2	0	1
3 - 2 -	4	2	0	0	0	0	0	1	0	1
3 - 3 -	4	2	0	0	1	0	0	0	0	1
3 - 4 -	2	3	0	0	0	0	0	2	0	0
3 - 9 -	2	2	0	0	0	0	2	3	0	0
3 - 25 -	0	1	0	0	0	0	7	6	1	3
3 - 27 -	1	0	0	0	1	0	0	0	0	1
3 - 31 -	1	1	0	0	1	1	1	1	1	0
4 - 2 -	2	2	0	0	0	0	0	0	0	0
4 - 4 -	4	0	0	0	0	2	0	1	0	0
4 - 5 -	1	0	1	1	0	0	0	0	1	1
4 - 6 -	2	1	0	0	1	0	0	1	0	0
4 - 7 -	2	0	0	1	0	0	1	2	0	0
4 - 8 -	0	1	1	0	0	0	1	1	1	0
4 - 13 -	2	3	0	0	0	0	0	0	0	0
4 - 18 -	0	0	0	0	0	0	0	3	0	0
4 - 21 -	0	3	0	0.	2	0	0	1	0	0
4 - 23 -	1	0	0	0	0	0	1	0	0	0
4 - 25 -	0	0	0	0	0	0	1	4	0	0
4 - 48 -	0	0	0	0	0	0	1	0	0	0
4 - 49 -	1	0	0	0	0	0	0	1	0	0
4 - 51 -	0	0	0	0	0	0	1	2	0	0
	33	26	3	2	6	3	25	35	8	11

DISTRIBUTION IN 1949

		HEREDITARY NERVE DEAFNESS				
AGE GROUP	NORMAL HEARING	HIGH TONE LOSS	MILD TONE LOSS	MODERATE LOSS	MODERATELY SEVERE	SEVERE
1 - 9						
10 - 19						
20 - 29						
30 - 39						
40 - 49						
50 - 59						
60 - 69						
70 - 79						
TOTAL 83	42	19	4	6	4	8

DISTRIBUTION IN 1960

		HEREDITARY NERVE DEAFNESS				
AGE GROUP	NORMAL HEARING	HIGH TONE LOSS	MILD TONE LOSS	MODERATE LOSS	MODERATELY SEVERE	SEVERE
1 - 9						
10 - 19						
20 - 29						
30 - 39						
40 - 49						
50 - 59						
60 - 69						
70 - 79						
80 - 89						
TOTAL 138	84	22	18	10	8	16

Figure 2

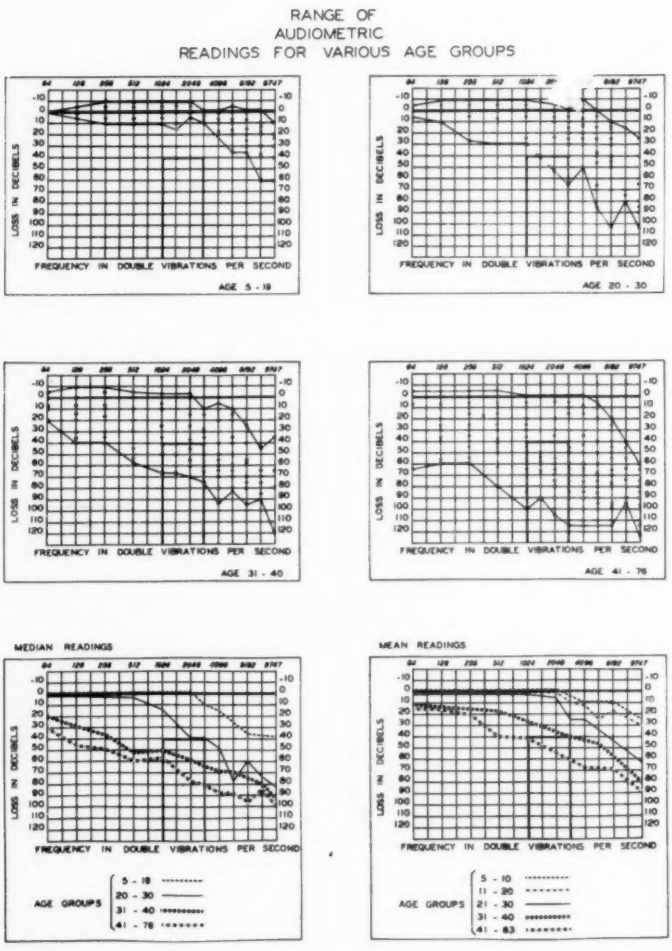
RANGE OF
AUDIOMETRIC
READINGS FOR VARIOUS AGE GROUPS
LOSS IN DECIBELS
FREQUENCY IN DOUBLE VIBRATIONS PER SECOND
AGE 5 - 19
AGE 20 - 30
AGE 31 - 40
AGE 41 - 78
MEDIAN READINGS
MEAN READINGS
AGE GROUPS
5 - 19
20 - 30
31 - 40
41 - 78
5 - 10
11 - 20
21 - 30
31 - 40
41 - 83

Figure 3

the reproducibility of the hearing tests, they were repeated after three months. The audiograms did not vary beyond five to ten decibels for any tone in any of the subsequent tests.

The first problem was to establish whether the loss of hearing was a consequence of impaired conduction or was of the neural type. Since air conduction was always better than bone conduction, and the audiograms showed the type of curve usually associated with presbycusis, it was concluded that the gene appeared to affect some portion of the neural mechanism.

Crowe et al.,[8] by means of testing, established the hearing in patients dying of intercurrent disease. After autopsy, they sectioned the temporal bones and found that in nerve loss in the higher tones, there was degeneration of both the sensory cells and nerve fibers in the basal turn of the cochlea.

The earliest manifestation of the hearing impairment appears as a high tone loss in children six to ten years of age (Figs. 2 and 3). It presents bilaterally, and usually progresses rapidly so that the affected members of the families become aware of their infirmity by their thirties when the loss had extended to the middle or speech tones. Deterioration spreads through the middle range synchronously with further loss in the high tones, until about the age of fifty. It is interesting that the progress of the impairment slows after fifty years of age, rarely approaching subtotal deafness.

Ten of the patients with severe hearing loss tested by monaural tone differentiation[3] showed no recruitment. Five cases were checked by the binaural test,[4] and also showed no recruitment. Fowler[5] showed that many ears showing recruitment also have poor auditory discrimination which is characteristic of an end organ disease in the cochlea.[6]

Twenty-three members of the kindred were tested for tone decay.[7] The method employed checked the tones of five hundred, four thousand and eight thousands vibrations per second. Although a few patients showed slight evidence of tone decay in the higher tones, by and large, there was no demonstrable evidence of nerve involvement.

The general pattern of this disease appears to be similar to that occurring with advanced age in normal individuals. One would like

to think of the gene as having the ability to change the rate of presbycusis rather than initiating a new process. This idea finds some support in the absence of recruitment or tone decay patterns. It is possible, of course, that the defect may be either in the organ of Corti, the nerve, or the central nervous system. As a convenient hypothesis, it may be proposed that the damage occurs most probably in the spiral ganglia.

SUMMARY AND CONCLUSIONS

1. Six generations of a family, comprising 349 members having hereditary nerve deafness, were followed for 14 years. They showed 71 cases representing the familial type of hearing impairment, and 20 children with high tone loss, believed to represent the early stages of the defect.

2. The trait appears to be the result of transmission of a simple dominant autosomal gene with complete penetrance.

3. As far as could be determined, no linkage relationships with other genetic traits could be established.

4. The hearing impairment was of a sensory neural type, with a high tone loss appearing in youth and spreading more rapidly than would be expected.

5. Recruitment was not found; and there was little evidence of tone decay, strengthening our previously expressed opinion that this process could be compared to premature aging.

2000 S. 9TH EAST ST.

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LXV

The Scientific Papers of the American Laryngological Association

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ANTERIOR OSTEOPLASTIC FRONTAL SINUS OPERATION

FIVE YEARS' EXPERIENCE

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The anterior osteoplastic approach to frontal sinus surgery has been previously described by Schonborn[1] and Brieger[2] in 1894 and 1895 respectively. It was later modified by Winkler,[3] Beck,[4] Hoffman,[5] Bergara,[6-8] Tato,[9] Gibson and Walker,[10] and Macbeth.[11] In the course of the many years which have elapsed since Schonborn and Brieger first suggested such an operation, much has happened to improve our surgical techniques. We have the benefit of antibiotic control of infection and we also have electrically operated instruments which make it much easier to cut a neat bone flap and thus obtain a precise reapproximation.

The purpose of this paper is to report our experiences with this procedure during the last five years at the Massachusetts Eye and Ear Infirmary, based on a "follow-up" study of our cases, some of whom have been previously presented in earlier articles.[12-14]

Those of us who have been brought up in the technique of the transorbital approach to the frontal sinus have believed that in order

to obtain a successful result, one should consider that the frontal sinus, the ethmoid and the sphenoid were a system of sinus cavities and that a very thorough cleaning out of all this area was essential to obtain a successful result. However, in the transfrontal approach, one treats the frontal sinus as a separate entity for the purposes of this operation. If the ethmoid also is to be operated upon, this can be done, as others have pointed out previously, by means of a transantral, combined transantral and intranasal or as in some of the cases to be reported by a transfrontal approach. The authors have found many cases also in which the ethmoid was not at all involved and in which the frontal sinus alone was affected. Of course, this would be the most favorable type for this operation.

The authors have felt that there were factors which were inherent in the transorbital approach, which tended to defeat its purpose. Stated briefly: in destroying the orbital wall, separating the nose from the orbit, the nasofrontal duct was also destroyed together with its lining membrane. In too many cases, which were followed over a period of years by several of the Staff[15,16] of the Massachusetts Eye and Ear Infirmary, it was found the fibrosis which formed in the region of the new surgical nasofrontal duct prevented drainage from the sinus. In fact, there were too many occasions for secondary operations in our series to make one feel really happy about this procedure. The studies of Walsh[17] and Hilding[18] show that the mucous membrane which lines the nasofrontal duct exerts a very positive drag on the mucous mantle within the sinus and that it is this movement of the mucus propelled by the cilia which is a most important factor in removing secretion from the sinus, and therefore not only the bony duct, but its mucosal lining should be preserved in cases not suitable for ablation.

Where there is structural abnormality in the sinus, such as osteoma, fronto-ethmoid cell narrowing, the nasofrontal duct, or mucocele or pyocele, the situation is an ideal one for the osteoplastic approach as it permits the removal of the pathology and entails no interference with the normal membrane which lies within the sinus nor with the nasofrontal duct. This technique is comparable to opening the lid of a box, removing an object from within it and closing the box. There is no destruction of anatomical boundaries nor interference with the physiology of the sinus membrane.

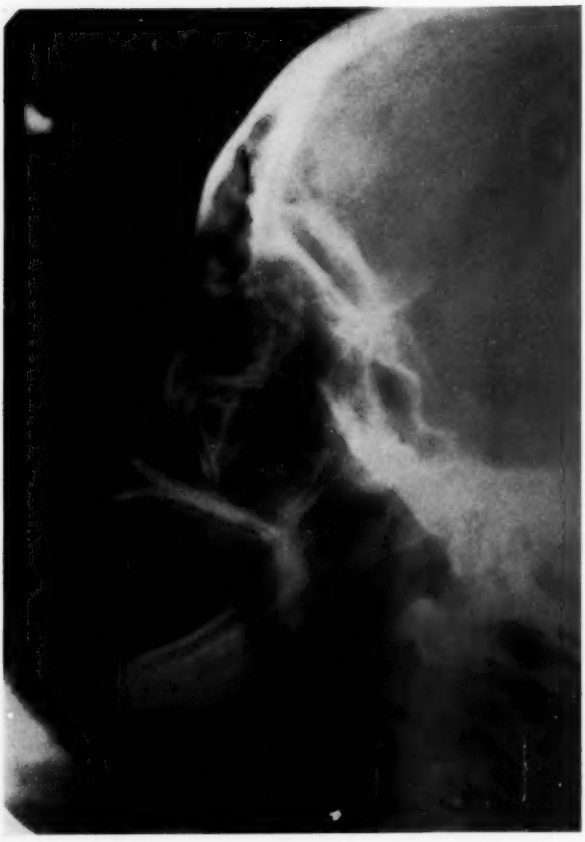

Fig. 1.—Case 1. Mrs. H.C. Postoperative x-rays 1961. This patient had an autogenous fat implant in the right frontal sinus after removal of all mucous membrane by curette and electric burr. Note that although the anterior wall bone flap has healed solidly, the fat implant has not calcified.

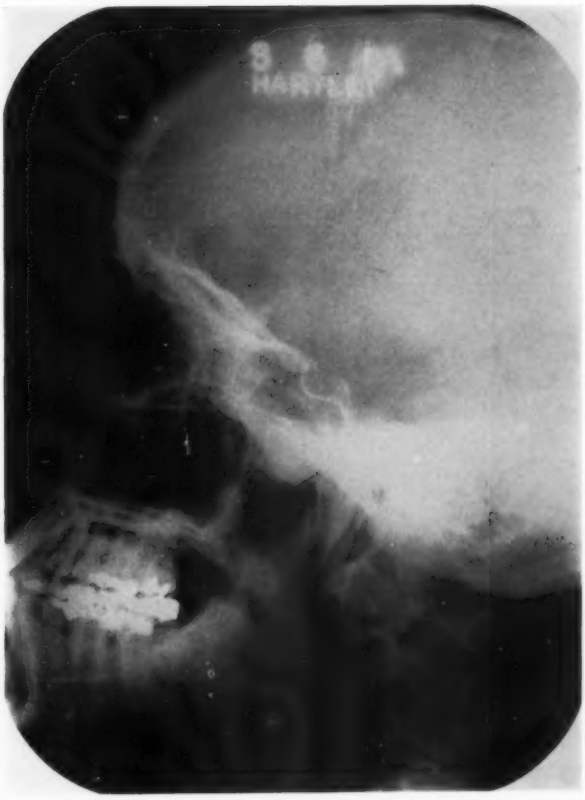

Fig. 2.—Case 4. Four years postoperative, 1961.

This approach lends itself equally well to the eradication of severe chronic disease in which there is no hope for restoring the mucous membrane to a normal condition and where there is no possibility of preserving or reconstructing a nasofrontal duct. In former times, the authors used the destructive technique of Riedel[19] which removed the anterior wall and the floor and the entire mucosal lining and collapsed the soft tissues of the anterior wall of the forehead

against the posterior wall. Although this was a disfiguring operation, it could be repaired very successfully by a secondary plastic insert of bone from the iliac creat. The anterior approach offers an even better way of obtaining obliteration without disfigurement. The anterior wall, after the removal of the pathology, is returned to its original position thus preserving the normal contours of the forehead. Likewise, as has just been mentioned, the orbit is not traumatized surgically. There is no disturbances of the pulley and therefore no secondary diplopia, which sometimes occurred in both the Lynch[20] and Riedel[12] type of operation. The main points to be considered in the obliterative operation by the anterior approach are that the mucous membrane must be completely removed and the nasofrontal duct occluded. In doing this, the authors use not only the curette to remove tissue, but also the electric burr whereby the microscopic remnants of membrane which would often elude the operator as they were so small, are actually ground away from the bone. In approaching the nasofrontal duct, the membrane is cut away and the lining of the duct is pushed downward into the nose. The bony walls of the duct are curetted, they may even be lightly burred to insure removal of membrane here also. The cavity is then filled with a small block of fat taken from the abdominal wall, preferably with some of the rectus aponeurosis attached to it after the techniques of Bergara[6-8] and Tato.[9] The fat is trimmed so that it will fit snugly into the frontal sinus cavity and the anterior wall is then returned to its original position and the wound closed.

TECHNIQUE

The instruments for this operation include those usually provided for any radical external frontal sinus operation. The electrically driven drills and burrs, such as are used in the present day mastoidectomy, and the Stryker saw are essential to this technique. In the first four cases, the senior author (RLG) used a small circular saw for cutting the osteoplastic flap. Subsequently, both authors have used the Stryker saw as there is less danger of the saw cutting soft tissue. If the frontal sinus is very shallow, or if there should be a dehiscence of the posterior wall, some damage might be done to the dura. This danger is obviated by the use of the Stryker saw.

X-rays taken in the lateral, Waters, fluid level, and the frontal views, give the most accurate estimate of the size and depth of sinus,

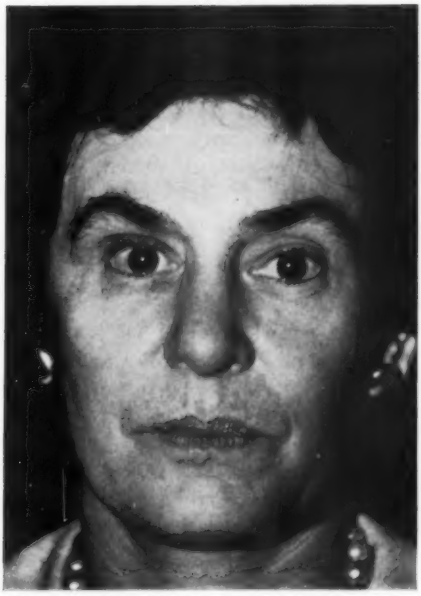

Fig. 3.—Case 4.

the position of pathology within the sinus and also a means for accurately measuring the outline of the sinus. We cut out of the frontal view film a pattern to show exactly the size and shape of the frontal sinus. We trim this pattern a little closer so that we may be certain that it is slightly smaller than the actual sinus. It is sterilized in aqueous zephiran so it can be handled safely at the time of the operation by the surgeon. Prior to the incision, this cutout is placed on the forehead of the patient to coincide exactly with the position of the frontal sinus, and a few light scratches are made with the scalpel in the skin around the periphery of the cutout to help as a guide later in determining the position for the cut in the bone. The patient is in a supine position with the forehead in a horizontal plane in order to obtain the best view of the sinus when the flap is turned down. The area is sterilized with aqueous zephiran and the patient is draped in the usual manner as for any frontal sinus surgery. The eyelids on

both sides are sutured in order to protect the eye from accidental contact with instruments. In our experience, it is best to have the anesthetist on the patient's left. The surgeon and his assistants then are free to move on the right side of the table and to the head of the table. Later, the view of the cavity from the head of the table is extremely important as it allows one to look directly downward into the nasofrontal duct and examine the floor of the frontal sinus most advantageously. The eyebrows are not shaved. The area of the incision is then infiltrated with 2% procaine and 1:50,000 epenephrine to reduce the tendency to bleed. As we all know, there are many blood vessels in this area and one should have a generous supply of hemostats to control bleeding. All bleeding must be controlled before the sinus is opened.

It is a general principle, we believe, that the incision should be sufficiently long to allow unhampered operating in the field. Too small an incision means excessive retraction of soft tissues with subsequent injury and an inadequate exposure of the frontal sinus so that later removal of pathology is difficult. We like to carry the incision from the midline along the upper margin of the eyebrow outward in a straight line to slightly beyond the outer limit of the frontal sinus. This incision is carried downward to the periosteum, but great care is taken not to cut through the periosteum, as it is important to preserve the blood supply of the bone flap. The soft tissues are then elevated from the periosteum upward so that an area is exposed somewhat beyond the limits of the frontal sinus. The pattern cut out from the x-ray is then re-applied and the incision is outlined along the upper margin of the cutout. A semicircular incision is then made down to the bone starting from the medial limit of the frontal sinus. This incision marks the position of the bone cut. With either the circular saw or the Stryker saw, the bone is then cut through this incision on the bevel downward in such a way that the bony edges, when the flap is replaced, will slightly overlap. As one approaches the medial and lateral ends of this bone cut, one encounters the harder bone of the supraorbital ridge. This may be cut with the saw or by the chisel. The chisel is then inserted above through the bone flap into the frontal sinus and with a gentle lift it is determined whether the flap is freely movable. Usually it is very movable. It has been suggested that in turning the flap down, dangerous lines of fracture might be produced in the roof of the orbit, but in our experience this

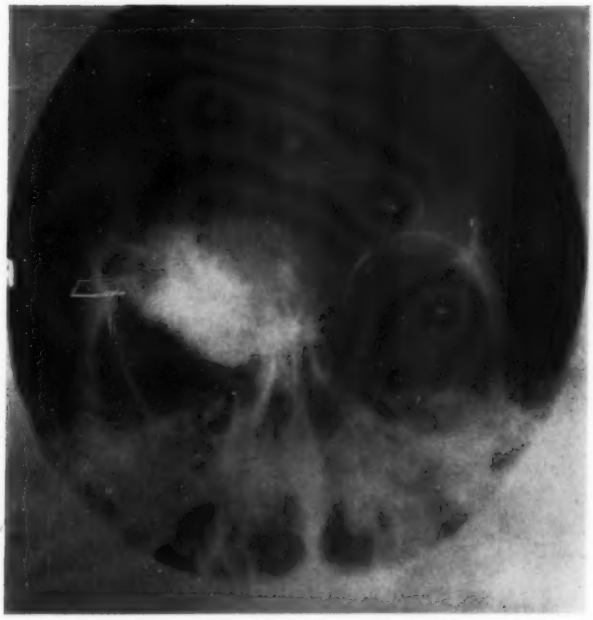

Fig. 4.—Case 6. Pre-operative.

bone is so thin that it cracks in a green stick manner without any displacement whatsoever.

This technique gives the operator complete freedom of choice, at this point, as to what further procedure he wishes to perform, either total obliteration with fat implant or the removal of local lesions within the sinus. It gives him a direct visual approach to the nasofrontal duct. We have used this approach for the removal of osteomata, fronto-ethmoidal cells, pyoceles and mucoceles where the sinus is only affected in part. Where the nasofrontal duct with its membrane and the remaining mucous lining of the sinus appeared to be normal, these areas can be left untouched. In a few cases, we have operated where a previous Lynch procedure had failed because of fibrous occlusion of the nasofrontal duct and in a few of these, we

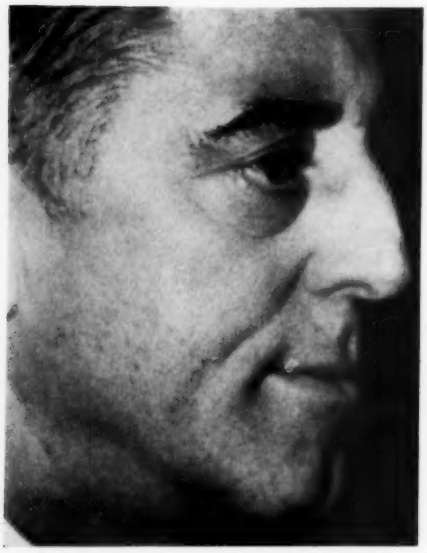

Fig. 5.—Case 6. A.D. Osteoma right frontal sinus. Postoperative photograph, 1961. Note absence of pre-operative displacement of right eye by osteoma.

have had to enter the sinus on the opposite side by taking down the interfrontal septum in order to provide drainage by way of the opposite duct. This has violated the principle, which we were taught, that we should never open a normal sinus for fear of infecting it. It is interesting that in our experiences this infection of the opposite side has not occurred.

Now, if one has to proceed to the removal of the entire mucous membrane and the complete destruction of the frontal sinus cavity, it is quite simple to dissect away all the membrane that can be removed by curette and periosteal elevator and then grind away the microscopic mucous membrane remnants with the electric burr. As the sinus is wide open, it is very easy to carry the burr around, under any overhang, into any crevice and to take down any partial partition and even to enter the nasofrontal duct to remove the membrane. At this

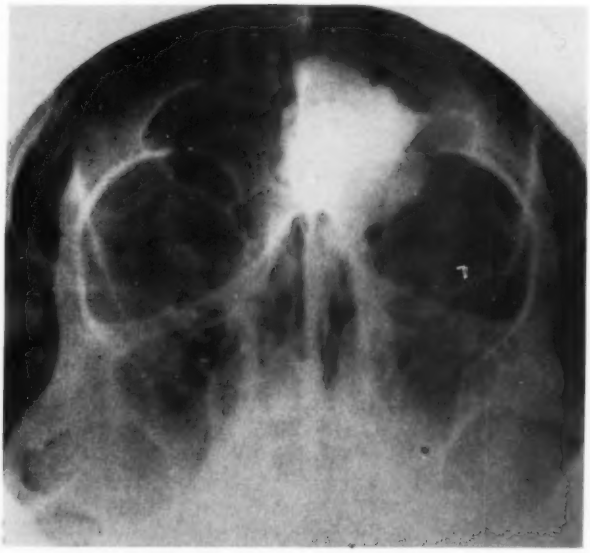

Fig. 6.—Case 7. Pre-operative.

point, the assistant drops out and changes gown and gloves. With an entirely fresh set of instruments he makes a small incision in the abdominal wall, usually in the right or left rectus area and obtains a block of fat as close to the muscle as possible, preferably with a little of the rectus muscle aponeurosis. The block should be just large enough to fill the sinus. The bone flap is turned back into place. After the fat has been inserted in the cavity, it is generally advisable to suture the periosteal incision with two or three absorbable sutures. The soft tissues overlying the periosteum are then returned to place and the wound is closed. A light pressure dressing is applied. The lid sutures are then removed. In all cases, we have found that the wound heals without complication. In four or five days, the sutures may be removed and very light dressing applied.

Since our first operation in 1956, the scope of this approach has been extended to cases of bilateral disease and to cases which had had intracranial complications.

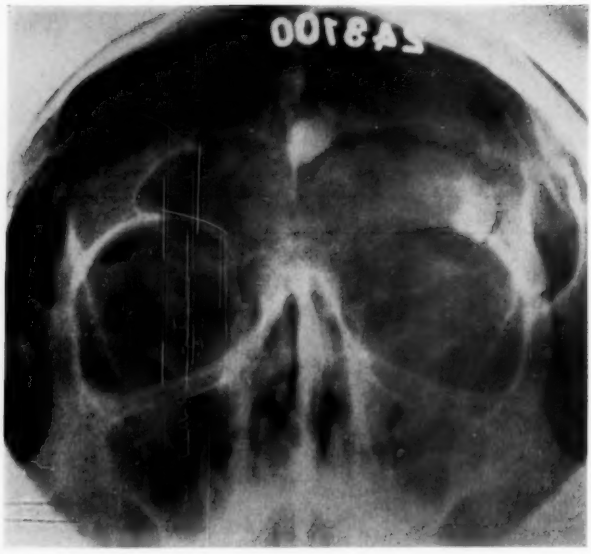

Fig. 7.—Case 7. Postoperative, 2 years.

The first operation that was undertaken was on the 19th of June, 1956. Thirty-one cases have been done by the authors and by other members of the Massachusetts Eye and Ear Infirmary Staff. We wish to thank them for an opportunity to include their cases in the overall statistics of this series.

When Beck[4] described his operation in 1908, objections were raised that there would be considerable danger of causing bone infection, even osteomyelitis, by cutting through the anterior wall of the frontal sinus and that it would be very difficult if not impossible to obtain a good approximation of the bone flap subsequently. This objection has been entirely removed, we believe, by the use of the electric saw and by cutting the bone on a bevel so that the edges overlap slightly when the flap is returned to its original position. The infections so feared prior to antibiotic treatment, have not appeared and so far we feel there is no danger from secondary infection. In

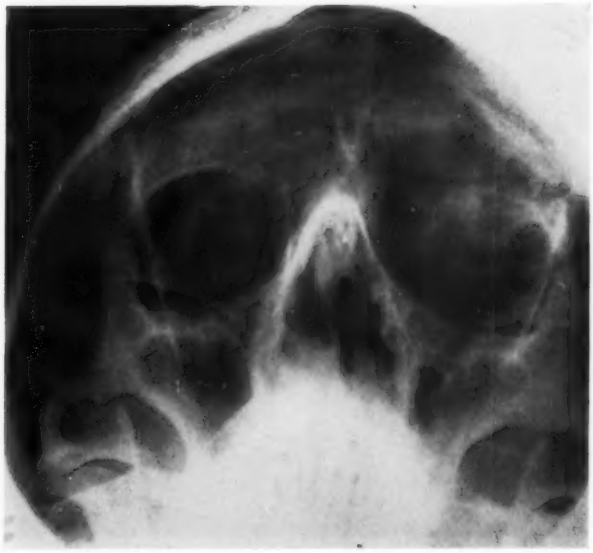

Fig. 8.—Case 8.

two cases, postoperative hematoma occurred both in the frontal area and in the abdominal wound and required aspiration. However, no infection occurred and there was no loss of fat from the frontal area and the wounds eventually healed up without any sign of complication. In two cases, there was a leakage of the lipoid element of the fat implant through breakdown of a suture, thus causing a temporary fistula. Here again, although the recovery was somewhat delayed, there was no loss of fat stroma and no collapse of the sinus. So far as can be determined, the fat is still in place although it is minus some of its lipoid content. The fear of infecting a healthy side by removing the interfrontal septum has not been substantiated. In two cases where autogenous fat was used and where x-ray follow-up has been done for 4½ to 5 years, no evidence of calcification has been noted. Bergara used "boilet fat," probably not autogenous, and reported calcification. One case is calcifying without tissue implant. Two cases have been reported at the Massachusetts Eye and Ear Infirmary

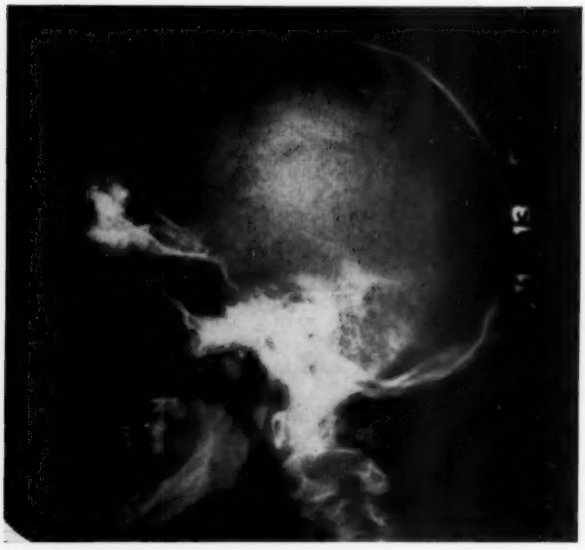

Fig. 9.—Case 9. Pre-operative x-ray.

with similar spontaneous calcification, one without operation and another after a Lynch operation.

This report is a follow-up study of six cases by R. L. Goodale and four cases by W. W. Montgomery. They have been selected from the series to illustrate the various types of pathology to which this technique is applicable.

REPORT OF CASES

CASE 1. Mrs. H.C., aged 36. Patient had had a long history of frontal headache due to right frontal sinusitis. The x-ray showed chronic right frontal sinusitis. The rest of the sinuses were clear. A right Lynch frontal sinusotomy was performed in 1953. In 1955, she required an incision and drainage for empyema of the right frontal sinus. On the 19th day of June 1956, an anterior osteoplastic frontal sinusotomy with an implant of abdominal fat was done. Following the Lynch operation, she developed diplopia. However, following the

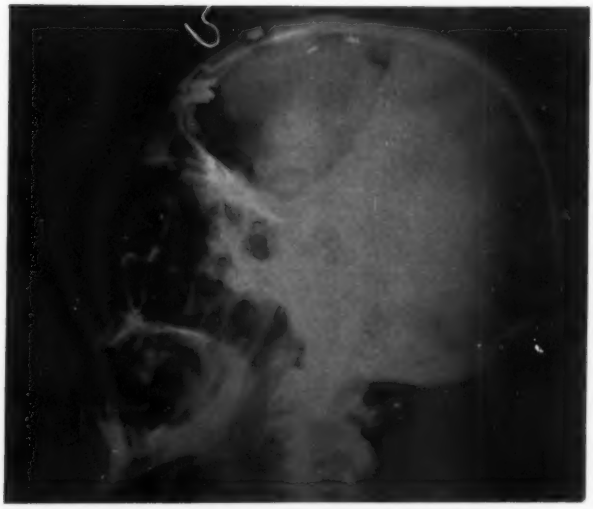

Fig. 10.—Case 9. Lateral x-ray after cranioplasty and removal of osteoma by osteoplastic approach.

osteoplastic operation, the diplopia was entirely relieved. She has had no further infection of the frontal sinus. Repeated x-rays to see if the fat, which was implanted, had calcified in the way that has been reported by Bergara, so far indicated that it has not occurred. However, the cavity has remained filled with fat. It is to be noted that the fat in this case and in subsequent cases to be reported is an autogenous tissue and not derived from a tissue bank. This is an obliterative procedure. The latest x-ray, on February 11, 1961, shows that the bone incision is well healed and in good position.

CASE 2. Mrs. M.M., aged 57. Patient came into the Massachusetts Eye and Ear Infirmary prior to 1950 with a long history of frontal and maxillary sinus infection. A submucous resection and bilateral Caldwell Luc operation were done in 1949. A right Lynch frontal sinusotomy was done in 1950 and again in 1951. As she continued to have reinfection of the right frontal sinus, an obliterative procedure was undertaken in 1953 with implant of bone taken from

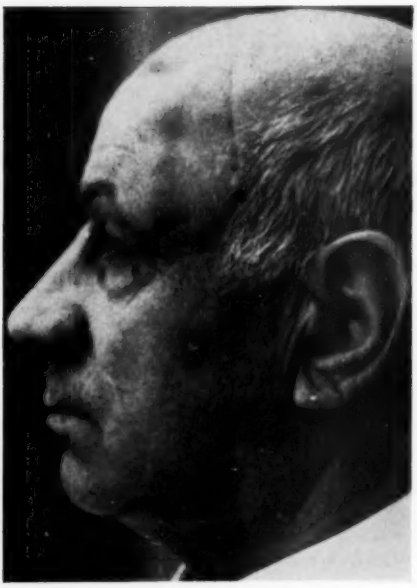

Fig. 11.—Case 9. Postoperative photo.

the iliac crest. Since then, there has been no further trouble with the right frontal sinus, although a few mucoceles have begun to appear according to the x-ray. The history of the left frontal sinus began in 1952 when it became acutely infected requiring a trephine. Again in 1956, the left frontal sinus became reinfected and another trephine was undertaken. This was followed by osteoplastic operation with fat implant on the 8th of November 1956. She has been followed ever since by x-ray and there has been no further infection of any of her sinuses. The postoperative x-ray in 1960 shows that there is good approximation of the bone flap and that the cavity is obliterated with fat. Again there is no evidence of the fat being transformed into bone.

Case 3. Mr. C.L., aged 58. Prior to 1957, patient had had a right intranasal anterior ethmoidectomy and enlargement of the naso-

Figure 12.

frontal duct. Since then, there has been repeated acute exacerbations of his frontal sinus infection eventuating in a pyocele occupying the lateral half of the frontal sinus. The floor of the frontal sinus was displaced downward so that there was considerable diplopia. On the 11th of January 1957, an anterior osteoplastic operation was done. The pyocele was found to be separated from the medial half of the sinus by a rather heavy cyst wall. This was removed and pathological tissue in the outer half of the sinus was likewise excised. As the medial half of the sinus and the nasofrontal duct seemed to be in good condition, patent and covered with normal membrane, no further removal of tissue was done. The downward bulging floor of the frontal sinus was pushed back into place by pressure from without in the method recommended by Goodyear.[21] Since then, he has had no further infection of his frontal sinus, no headache, no disturbance of vision and an anosmia which he had had previously also disappeared.

CASE 4. Mrs. P.H., aged 39. She had had repeated attacks of right frontal sinusitis, a right Lynch frontal sinusotomy was done in

1945. Following this, there were still many attacks of frontal sinusitis. She came to me (RLG) for re-operation on the 18th day of October 1957. At that time, there was a pyocele in the right frontal sinus. The floor of the sinus was bulging downward displacing the upper lid and the interfrontal septum was beginning to bulge into the left sinus. The flap was turned down revealing a large pyocele and a dehiscence in the interfrontal septum. The nasofrontal duct was completely occluded by scar tissue. Pathological membrane was removed where found and as the perforation already existed into the left frontal sinus, this was further enlarged by ronguers and burr, thus converting both sinuses into one cavity which drains now through the left side. The left frontal sinus has never become infected and the left nasofrontal duct seems to operate well, doing duty for both sides. Postoperative x-rays in 1961 show calcification on the right side which has begun to obliterate the cavity. This is spontaneous calcification without tissue implant.

CASE 5. Dr. R.E.P., aged 28 years. Acute left frontal sinusitis in February 1960, required a trephine. In the course of the follow-up x-ray, it appeared that he had a large osteoma occupying the anterior portion of the ethmoid, the adjacent frontal sinus and possibly encroaching upon the cribriform plate. What did not appear at the time but was subsequently discovered in reviewing the x-ray, was a very large fronto-ethmoid cell occupying the entire nasofrontal portion of the frontal sinus. An osteoplastic operation was done on the second of March 1960. It was at this time that the fronto-ethmoid cell was discovered. It was removed. The osteoma, being in a dangerous area and not actually obstructing the frontal sinus drainage, was not removed. He has been symtom-free ever since.

CASE 6. Dr. A.D., aged 50 years. An osteoma slowly had been developing in the right supra-orbital area for many years. Eventually this had encroached on the supra-orbital ridge of his frontal bone and the roof of the orbit, displacing the eye downward and outward and consequently causing marked diplopia. Other than this, there were no symptoms. The x-ray shows a very large osteoma occupying the entire right frontal sinus and encroaching upon the orbit and the supra-orbital ridge. Anterior osteoplastic frontal sinusotomy was done. The osteoma was very large. In removing it, it was necessary to cut it in two by means of the Stryker saw. Following this, the

osteoma came away very easily. It was found that the floor of the sinus and the supra-orbital ridge were defective. In spite of this, there is only slightly depression in this area and in the photograph there is no notable difference in the two sides. The diplopia has entirely subsided and the eye is back in its proper position.

CASE 7. W.D., a 37-year-old white male, was admitted in 1957 with a three-months history of diplopia and intermittent frontal headache. X-rays of his sinuses showed a very large osteoma in the left frontal sinus which markedly displaced the interfrontal septum to the right and was encroaching on the cribriform plate. The osteoma was removed by the anterior osteoplastic frontal sinusotomy technique. The sinus was not obliterated with fat because the nasofrontal duct was patent.

The x-ray demonstrates the outline of the osteoplastic flap and also the site of origin of the osteoma.

The patient has remained symptom-free for four years.

CASE 8. I.J., a 42-year-old woman, had onset of diplopia in 1947 due to a supra-orbital mass depressing the left eye. At this time a submucous resection of the nasal septum and a left external ethmoid were carried out. Two months later a left frontal operation was performed by the Lynch method. A revision was necessary one year later because of recurrent diplopia. In 1957, further revision of this left radical frontal was done to remove a pyocele in this sinus. Tantalum foil was sutured to the orbital capsule to keep the nasofrontal duct open. In 1958, the patient was admitted because of a recurrent pyocele. An anterior osteoplastic frontal sinusotomy was performed. The bony posterior wall of her frontal sinus was found to be nearly totally absent. The pyocele was removed intact. The mucous lining of the osseous walls of the sinus was taken away with a burr. The bone flap was replaced. There was no communication between the frontal sinus and the nose. No fat was inserted because the dura projected anteriorly and completely obliterated the sinus by contact with the anterior wall. The patient has remained symptom-free since this time.

CASE 9. F.P. This 54-year-old male was admitted in November 1959 to the Neurosurgical Department of the Massachusetts Gen-

eral Hospital with a one-week history of seizure, personality change and disorientation. X-rays showed a large osteoma in the frontal sinus which had grown through the posterior wall of the frontal sinus and into the frontal lobe, where a large encapsulated abscess had formed. He was operated upon in two stages.

On November 18, 1959, a large frontal lobe abscess was excised and a portion of the osteoma protruding into the frontal lobe was excised by cranioplasty. The dura was covered with a polyethylene sheet.

On December 30, 1959, the large osteoma was removed by way of a bilateral anterior osteoplastic frontal sinus procedure. The osteoma displaced 33 cc of water. The sinus was obliterated with abdominal fat. The last x-ray shows the patient's status one year following this procedure. A recent photograph of the patient shows little deformity following this extensive surgery.

CASE 10. P.D., a 48-year-old white male, underwent a left Lynch frontal sinus operation in 1939 for left pansinusitis. Two months following this procedure bilateral Caldwell Luc and ethmoidectomies were carried out. The patient did fairly well until 1959. A pyrocele of the left frontal sinus was diagnosed at that time. A revision was carried out and drainage was established with a portex nasofrontal tube. In less than one year following this the patient had developed a mucocele in both frontal sinuses. A bilateral anterior osteoplastic frontal sinusectomy was performed using abdominal fat to obliterate. The patient has remained well since this time. Recent photographs are shown to demonstrate the deformity on the left side resulting from the Lynch radical frontal sinus procedure and relatively little deformity on the right following the fat obliteration operation.

SUMMARY

Since 1956, upwards of thirty-one frontal sinus diseases of various types have been operated upon at the Massachusetts Eye and Ear Infirmary using the anterior osteoplastic approach. The authors have presented nine cases describing these conditions. Our conclusions are as follows:

1. This technique is applicable to the removal of localized pathology as well as to the obliteration of the frontal sinus.

2. In all cases, the problem of disfigurement has been eliminated.

3. There are distinct advantages in preserving the anatomical structures of the orbit.

4. In cases where obliteration is not indicated, the nasofrontal duct and the normal mucous membrane of the sinus can be preserved.

5. The use of the fat implant has been satisfactory. No secondary infections have occurred, and there has been no necessity for re-operation in these cases. X-ray evidence indicates that where fat has been used, this has remained unchanged and osteogenesis or sclerosis has not obliterated the cavity.

6. There is some evidence that where the entire mucous membrane has been removed without fat implant, osteogenesis does occur and tends to obliterate the cavity.

7. Removing the interfrontal septum in cases of unilateral disease has not affected adversely the normal side.

8. This technique has been usued successfully in cases of bilateral disease and in one case of intracranial complication.

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LXVI

THE ELECTRONIC SYNCHRON-STROBOSCOPE

ITS VALUE FOR THE PRACTICING LARYNGOLOGIST

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The social and scientific interest in human communications and the development of mass media during the past decades have directed increasing attention to the human voice and to the organ of voice production, the larynx. It would be a pleasure to record that this interest on the part of the lay public had been accompanied by a comparable advance in the diagnosis and treatment of laryngeal problems. However, throughout this period our specialty has been so attracted to the phenomenal discoveries for the surgical restoration of hearing, that in our offices we have concentrated mainly on apparatus for the investigation of the middle and inner ear.

As a result, most of us are still baffled by the disproportion between vocal symptoms and laryngeal findings. We still use our eyes for routine visualization of the larynx, although we may realize the inadequacy of this procedure. How can the human eye, whose perception is limited to five distinct images per second, evaluate the intricate vibrations of the vocal cords, which occur at speeds of 100, 500, or 1,000 excursions per second? This physical limitation in turn has prompted all of us on occasion to advise a patient that there is nothing the matter with his larynx when it is obvious that there must be some reason for this hoarseness. Would we be wrong in comparing our approach to that of an otologist who employed only his visual acumen in the evaluation of deafness and ignored audiometric and other special tests?

The limitations of our vision are shown by a film of a patient with unilateral vocal cord paralysis. The left vocal cord remains in the inter-

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From the Institute of Laryngology and Voice Disorders and Northwestern University Medical School.

mediate position indicating a paralysis of central origin; the involved cord appears virtually at a standstill (Fig. 1A). Now observe the same picture in ultra slow motion. Note the vigorous excursions of the paralyzed vocal cord during each vibratory cycle (Fig. 1B)—an amazing transformation! Since the production of voice and hoarseness are directly related to vibratory phenomena, the importance of accurate observations requires no further emphasis.

How can the clinician perform this service for his patient in his own office, without the costly and time consuming medium of ultra high speed photography? The answer lies in the electronic laryngo-synchron-stroboscope, which meets the clinical requirements for the evaluation of vocal cord vibrations via indirect laryngoscopy under ordinary office conditions. For an explanation of this effect it becomes necessary to review briefly the principle of stroboscopy and the design of the electronic laryngo-synchron-stroboscope.

Stroboscopy produces an optical illusion in which an object moving rapidly and periodically appears to stand still, or move very slowly. This illusion is obtained by the intermittent but regular presentation of the object to the viewer. The phenomenon is based on Talbot's law, or the persistence of vision in the human eye, which causes each image to linger on the retina for 0.2 seconds after the exposure.

If we apply this principle to the vibrating vocal cords, the rapid movements appear to be arrested or greatly slowed. Synchronization of the illumination with the frequency of vibration results in an apparent standstill of the vocal cords in any desired position, thus permitting accurate inspection of the phonating structures (Fig. 2). To obtain a slow motion effect of the vibratory cycle, one needs only to vary the rate of illumination slightly in relation to the frequency of vibration, so that each successive light impulse strikes a different phase of the vibratory cycle (Fig. 3).

Theoretically, this intermittent effect may be produced a) at the source of illumination, b) between the illumination and the eye, c) at the eye, and d) between the eye and the vibrating vocal cords. Historically, all of these possibilities have been explored.

Towards the end of the 19th century, Oertel[1] described a stroboscope for laryngeal observations, which was based on the regular inter-

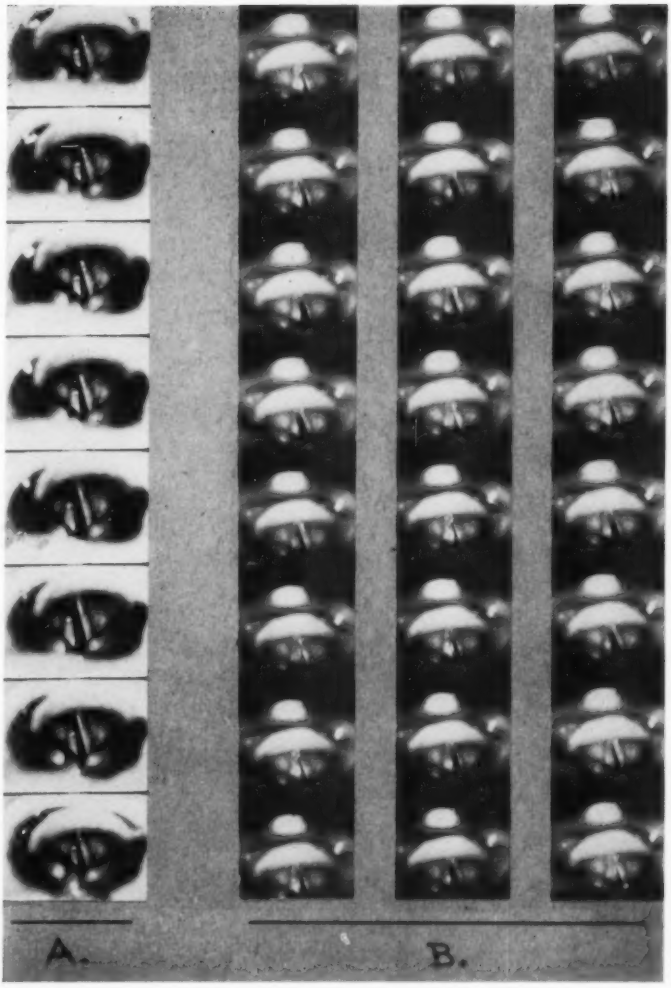

Fig. 1.—Sequence from motion picture of unilateral vocal cord paralysis during phonation. A) Normal speed: the right cord moves freely, while the left vocal cord remains in the intermediate position, apparently motionless. B) Ultra high speed: the vigorous excursions of the paralyzed vocal cord can be clearly observed during each vibratory cycle.

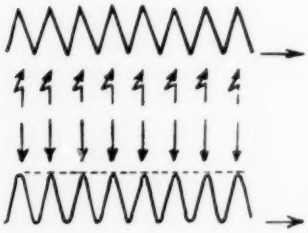

Fig. 2.—Schematic drawing of stroboscopic effect (after Schönhärl). The synchronization of the illumination (upper graph) with the frequency of vibration (lower graph) results in an apparent arrest of motion.

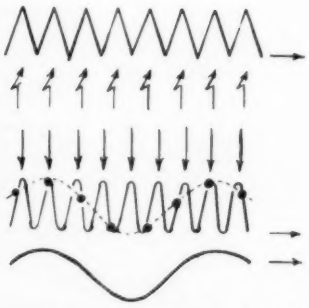

Fig. 3.—Schematic drawing of stroboscopic effect (after Schönhärl). A slight variation in the relative frequencies of the illumination (upper graph) and vibration (middle graph) produces slow motion effect (lower graph).

ruption of the light beam by a perforated disc (Fig. 4). This ingenious invention was developed further by numerous scientists including Hegener,[2] Panconcelli-Calcia[3] and Loebell[4] in Germany; Stern[5] in Austria; Tarneaud[6] in France; and Kallen,[7] Powell,[8] and Andrews[9] in the United States. Unfortunately, the disc stroboscope produced as much criticism as praise, and as a result, this very promising method of examination was discarded before it became widely used.

Many of you remember the justifiable complaints against this method of examination. To mention but a few: objectionable background noise, frequency disturbances with slight variations of electric potential, the difficulty of maintaining the same pitch for prolonged periods, decrease in illumination with increasing frequency, the necessity of changing discs to vary frequencies, and other technical or extraneous difficulties.

Above all, the disc stroboscope called for a trained subject or at least a musical patient who could duplicate and maintain the specific pitch corresponding to the speed of the rotating disc. Small wonder, therefore, that the inexperienced observer did not know whether to ascribe visible irregularities to the apparatus or to his patient, and eliminated this temperamental equipment from further consideration.

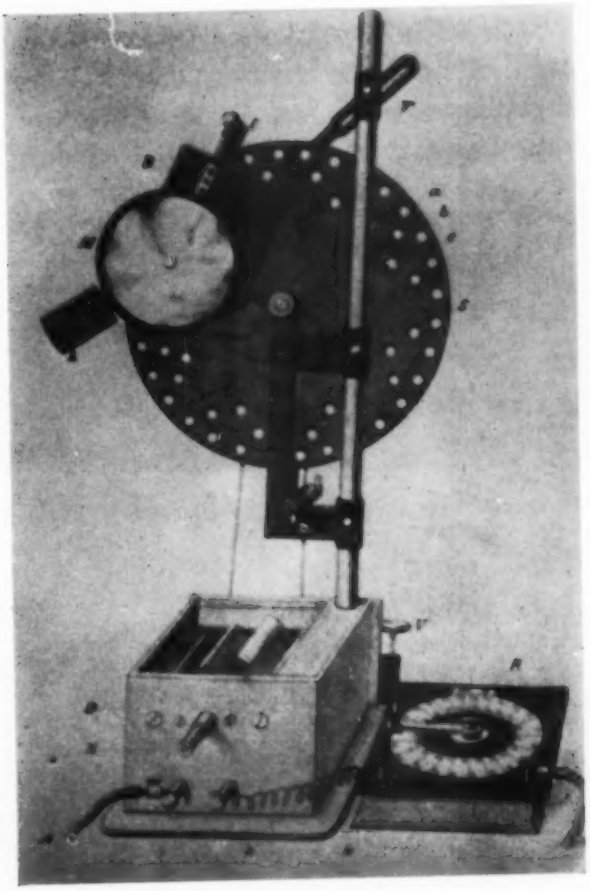

Fig. 4.—Oertel's disc stroboscope.

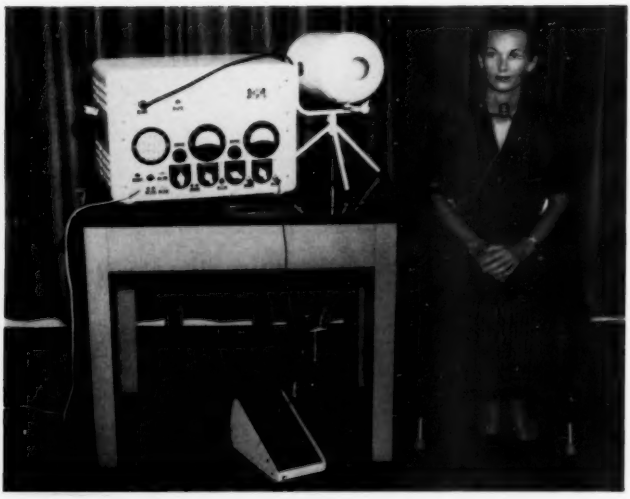

Fig. 5.—Electronic laryngo-synchon-stroboscope (Model Timcke KS-3) showing microphone in position, electronic unit, Xenon lamp and foot pedal.

More recently, the field of laryngeal stroboscopy has progressed along an entirely different direction.[10-13] The development of powerful gas discharge tubes provides an intensive intermittent beam of light, with sharp flashes at any desired frequency. Electronic connections permit automatic synchronization of the rate of illumination with the pitch or frequency of vocal cord vibrations. This new approach, then, eliminates the admitted faults of the disc stroboscope and provides a simple and effective method for stroboscopic examination of the larynx.

Prominent laryngologists and voice scientists in different countries grasped the potential of this new diagnostic tool, and during the past decade a series of different electronic stroboscopes have been designed specifically for laryngeal examinations.[14-19] After an evaluation of instruments produced in the U.S.A., Germany, France, Scandinavia, The Netherlands, The Argentine and Mexico, I have come to the conclusion that two of these new electronic stroboscopes are super-

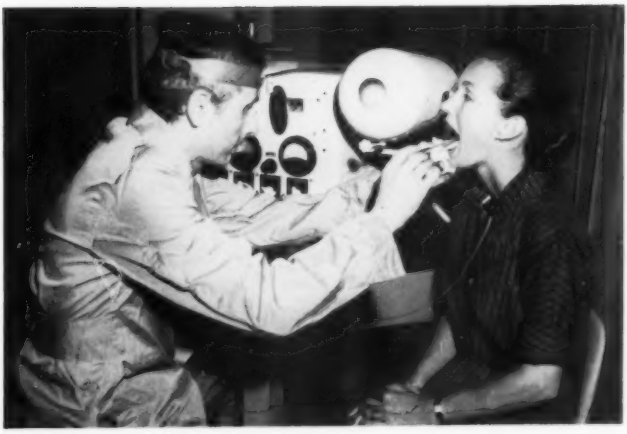

Fig. 6.—Typical stroboscopic examination via indirect laryngoscopy.

ior for an evaluation of laryngeal conditions: 1) the stroboscope designed by Dr. Jw. van den Berg[20] at the University of Groningen, which is manufactured by the Phillips Company in The Netherlands, and 2) the stroboscope designed and manufactured by Dr. Rolf Timcke[21] at Hamburg, Germany. These instruments employ the same general principles; since Dr. Timcke perfected his equipment at our Laryngeal Research Laboratory, I am more familiar with its design, and my subsequent remarks will be limited to this unit.

Timcke's original laryngo-synchron-stroboscope (Fig. 5) consists of four separate parts: the microphone, the light source, the electronic control unit, and a foot pedal. The microphone, which is applied to the patient's neck just below the larynx, directs the sound waves to the electronic control unit where they are filtered and amplified. The fundamental frequency of the sound produced in the larynx is transmitted via electronic pulses to a Xenon lamp which emits an intermittent beam of white light at the same identical rate. Thus the frequency of the light flashes always corresponds to the frequency of vocal cord vibrations, regardless of pitch or pitch change. The light beam is directed by an ordinary head mirror to the laryngeal

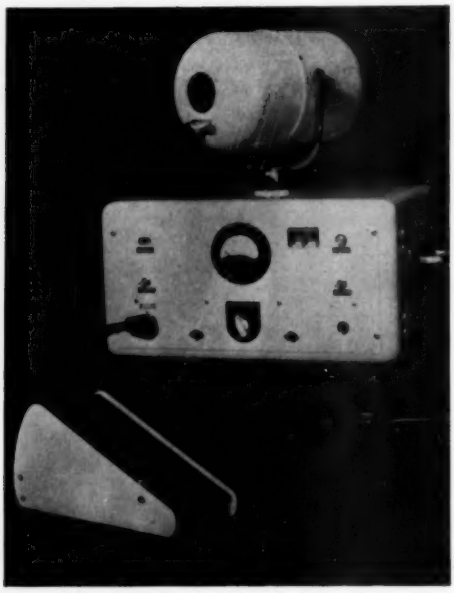

Fig. 7.—Clinical electronic synchron-laryngo-stroboscope (Model Timcke KS-4) showing throat microphone, Xenon lamp mounted on control unit and foot pedal.

mirror and thence to the larynx, as in any indirect laryngoscopy (Fig. 6).

A semi-automatic auxiliary light system permits illumination of the larynx before voice production, while the examiner adjusts his head mirror and prepares for the examination. Meters on the instrument panel indicate the fundamental frequency from 65 to 1,000 vibrations per second and the intensity of phonation. The frequency of light flashes can also be controlled directly with a built-in audio frequency generator, if an aphonic or nearly aphonic patient is unable to maintain a satisfactory sound. The foot-pedal permits a change in the phase angle of the light flashes in relation to the sound

impulses to obtain either a stationary image of the vocal cords at any instant of their vibration, or the typical slow motion effect.

Additional attachments permit automatic recording of frequency and intensity variations, faradization therapy, and photography of the phonating larynx. It is apparent that this instrument was designed for experimental use as well as routine clinical observation. In order to produce a simpler and less costly instrument for the practicing laryngologist, Timcke also manufactures a smaller unit (Fig. 7). This apparatus functions on the same basis as the larger equipment and includes all the facilities required for clinical examinations, e.g. throat microphone, pitch indicator, phase variation, auxiliary illumination.

What information may the clinician expect from the employment of this equipment and how can he utilize this knowledge in the practice of laryngology? Other methods of examination, indirect laryngoscopy and direct laryngoscopy, seem to supply adequate information regarding organic lesions of the larynx and permit an accurate interpretation of organic laryngeal disease in most instances. However, any observation which depends upon the unaided human eye is limited to gross movements; in the case of the larynx the traditional forms of examination demonstrate only the gross activity of the arytenoid cartilages and intrinsic laryngeal muscles, and the conductivity of the major laryngeal nerves.

A stroboscopic inspection, on the other hand, affords a glimpse at the larynx in action and rewards the patient observer with valuable information regarding the minute details of laryngeal vibrations. These vibrations in turn depend on 1) the structure of the vocal cords, which is affected by inflammation, infiltration, neoplasms, etc., 2) the tension of the vocal cords, which may be influenced by unusual contractions or paralyses, 3) the condition of the mucous membrane which plays such a complex and vital role during the period of approximation, and 4) the degree of subglottic pressure.

A typical stroboscopic evaluation utilizes both the still and slow motion effects of this technique. The moving picture presents a general orientation regarding the functional adjustments of the vocal cords and the ability of the patient to maintain a constant tone. It also affords information regarding the relative excursions of the

two vocal cords and phase variations within the vibratory cycle, at different levels of pitch and intensity.

The still picture presents a sharp and clear image of the vocal cord margin during the different phases of the vibratory cycle, in contrast to the diffuse blur visible to the naked eye. Deliberate phase variations of the still picture through the full cycle of 360 degrees demonstrate fine details of laryngeal activity, including muscular and mucosal abnormalities, directional changes, or differences in amplitude and approximation. Such minor details of laryngeal behavior are of definite clinical significance, because they may be associated with qualitative changes in the human voice—hoarseness, harshness, breathiness, weakness, etc. Singers, for instance, often become aware of the slightest functional abnormalities, which are indistinguishable to the untrained ear.

The electronic laryngo-synchron-stroboscope thus offers a simple technique of differentiating physiologic and structural abnormalities of the larynx. In many instances the same examination affords valuable etiologic clues and facilitates the choice of the appropriate therapy. Follow-up examinations permit an accurate evaluation of the patient's progress under treatment. With the addition of the pulse current apparatus, the instrument can also be used for physical therapy, i.e. accurate harmonic stimulation of a diseased vocal cord.

Since the introduction of this modern electronic equipment, more and more laryngologists have adopted this technique for routine laryngeal examinations. It would be difficult to find a major laryngeal center on the continent of Europe without at least one electronic stroboscope. Our South American colleagues are following this example. By contrast, there are but five such instruments in regular use in the United States, and to the best of my knowledge none in Canada or the United Kingdom. It is not surprising, therefore, that little information regarding this technique has been disseminated through the recent English literature. However, laryngologists with a reading knowledge of the German language will find a wealth of useful information in a recent book by Dr. Elimar Schönhärl,[22] who has pioneered this area.

I have used such an instrument in my office for the past four years, and would not wish to practice laryngology without it. In many instances, my stroboscopic examination has obviated the neces-

sity for a direct laryngoscopy, with its attendant cost and discomfort to the patient. A complete stroboscopic examination should not exceed ten minutes, if one works with a co-operative patient. It is scarcely necessary to mention to this audience of laryngologists that an understanding of the technique and a familiarity with the normal vibratory pattern of the vocal cords are prerequisites for the interpretation of abnormal findings.

After an evaluation of the case histories of several hundred patients, I have been impressed by the following specific diagnostic advantages of my electronic laryngo-synchron-stroboscope:

1) *The Diagnosis of Functional Disorders of the Larynx.* Functional hoarseness and weakness of the voice present a real challenge to the laryngologist. The electronic laryngo-synchron-stroboscope is the only office equipment which permits an accurate evaluation of these cases, and affords controlled supervision during therapy. In many cases changes in pitch, tension, or intensity minimize an abnormal pattern of vibration, a valuable aid in outlining indicated therapy.

2) *The Extent of Organic Disease.*. The slow motion effect of the stroboscopic examination permits differentiation between superficial lesions of the mucous membrane and deeper lesions involving the underlying structures, without biopsy. There is little difficulty in distinguishing an edematous nodule which is likely to respond to voice therapy, from a fibrosed node requiring surgical excision. The extent of polyps, cysts, and other benign tumors can be determined satisfactorily before definitive surgery.

3) *The Differentiation Between Benign and Malignant Tumors.* The unilateral absence of vibration on stroboscopy often permits the early diagnosis of a malignant lesion, long *before* the unaided eye detects any limitation of motion.

4) *The Degree and Prognosis of Laryngeal Paralyses.* Stroboscopic inspection affords valuable information regarding the type and degree of laryngeal paralyses; it permits a differential diagnosis between a unilateral paralysis and ankylosis of the crico-arytenoid joint. A return of the typical mucosal pattern on the involved side usually represents the first indication of recovery.

5) *The Evaluation of Laryngeal Trauma.* Changes in laryngeal vibrations indicate the degree of trauma, and assist in the selection of indicated therapy and in the termination of voice rest. The resolution of extravasations and the disposition of scar tissue often produce persistent hoarseness without gross evidence of injury. The abnormal vibratory pattern, however, permits an objective confirmation of the vocal changes, and assures an accurate medico-legal evaluation of the impairment.

SUMMARY

The electronic laryngo-synchron-stroboscope provides an efficient and effective diagnostic tool in office laryngology. A stroboscopic examination provides valuable information regarding functional diseases of the larynx, the differentiation between benign and malignant tumors, and the etiology, extent, and prognosis of various benign lesions. The value of this equipment for physical therapy requires additional investigation.

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LXVII

SARCOMA OF THE LARYNX

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Sarcoma of the larynx is an uncommon lesion, probably comprising less than one per cent of all malignant tumors of this organ. A recent review of the English literature by Kratz and Ritterhoff[8] showed a total of seventy-one cases, of which twenty-six had been previously reported or reviewed by Havens and Parkhill.[6] Sarcoma apparently is more common in males than in females, though to a less striking degree than carcinoma, and although the predominant incidence is in the later decades, Rigby and Holinger[11] report a fibrosarcoma in a young infant.

From the histogenetic point of view, one must recognize the possibility of the occurrence of at least twelve types of malignant tumor of mesenchymal origin. However, the present report will deal with only those instances of sarcoma observed at the Chevalier Jackson Clinic during the years 1941 to 1959, inclusive. These include four cases of fibrosarcoma, one case each of neurogenic sarcoma, Hodgkin's sarcoma and reticulum cell sarcoma, and two of so-called "carcinosarcoma" in which both carcinomatous and sarcomatous elements were found; both of the latter cases are more likely instances of the pseudosarcoma described by Lane[9] and by Baker,[2] but are included for comparison.

Criteria for the recognition of these tumors based on gross appearance are difficult to define, because of the variability encountered, even in lesions of similar histologic type. In each of the cases briefly described, the laryngoscopic appearance of the lesion is given,

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and in four of those treated by operation, the surgical specimens are illustrated. The histologic features are exemplified in photomicrographs.

FIBROSARCOMA

The clinical behavior of the fibrosarcoma in general appears to reflect the histologic character of the lesion. The well differentiated fibrosarcoma is characterized by an abundance of fibrous stroma, with a relatively small cellular component in which the cells, though showing the usual criteria of malignancy, show less variation in size and shape than the more anaplastic tumors, which are relatively cellular, with a minimum of stroma, showing greater pleomorphism. Metastasis from the fibrosarcoma, when it occurs, is said to be nearly always by the hematogenous rather than lymphatic route. Metastasis of any type from a well differentiated fibrosarcoma is uncommon.

REPORT OF CASES

CASE 1. R.S., a white female 66 years of age, was referred for examination because of hoarseness of two weeks' duration. The laryngoscopic examination showed a rather smooth fusiform reddish elevation on the margin of the mid-portion of the right cord. The tissue removed for biopsy showed numerous spindle-shaped and pleomorphic cells with appreciable numbers of mitoses, and a surface covering of orderly squamous epithelium. Additional tissue was removed two weeks later with similar findings, and the diagnosis of a malignant tumor of mesenchymal origin was again returned. Because of the well localized and sharply marginated character of the lesion, the right vocal cord was removed by laryngofissure (Fig. 1).

Microscopic sections of the surgical specimen show a relatively abundant collagenous stroma, within which are spindle-shaped cells of varying size and shape with hyperchromatic distorted nuclei, mitoses and tumor giant cells. The pathologist's diagnosis was "low-grade fibrosarcoma." This patient is living and well without evidence of recurrence or metastasis, after six years and eight months, having been last examined on March 27, 1961.

CASE 2. H.F., a white female 65 years old, was first seen in February, 1942. Hoarseness had been noted about one year before,

and during the six months prior to our first examination, tissue had been removed elsewhere from the vocal cord on three occasions. The first two biopsies had been interpreted as fibroma and granulation tissue, respectively, but the tissue removed at the time of the third biopsy was diagnosed as a fibrosarcoma of well-differentiated type. Grossly, the lesion appeared to involve the anterior extremity of the left cord and the anterior third of the right, without extension above or below the cordal level.

A laryngofissure by the anterior commissure technique was performed by Dr. Chevalier L. Jackson, and microscopic examination of the surgical specimen confirmed the pre-operative diagnosis.

Histologically this was a tumor of somewhat more cellular character than that of the previous case. Otherwise, the histologic criteria for the malignant nature of the lesion are much the same. This patient was living and well after 12 years, without evidence of recurrence or metastasis.

CASE 3. W.C., a white male 63 years of age, was first seen in October, 1957, with a history of hoarseness beginning six months before. A lesion had been removed elsewhere from the right vocal cord shortly after the onset of symptoms, and the voice appeared quite normal for a period, when hoarseness recurred and a second biopsy was performed. The pathologist rendered a diagnosis of sarcoma, and the patient was referred for operation. On direct laryngoscopy, the right cord was found to be somewhat thickened, with a roughened appearance, extending from the tip of the vocal process to the anterior commissure. Motion of the vocal cord was not impaired.

A partial laryngectomy of the fronto-lateral type was performed on October 30, 1957, with excision of the entire right cord, a large portion of the arytenoid and a part of the ventricular band, along with the anterior extremities of the left cord and ventricular band and a vertical anterior segment of thyroid cartilage in continuity (Fig. 2). Convalescence was satisfactory, although some degree of webbing occurred anteriorly. There has been no evidence of recurrence or metastasis after three years and six months, up to and including the last follow-up visit on May 4, 1961.

Histologically, this appeared to be a tumor of moderate cellularity, with numerous atypical nuclei, mitotic figures and tumor giant

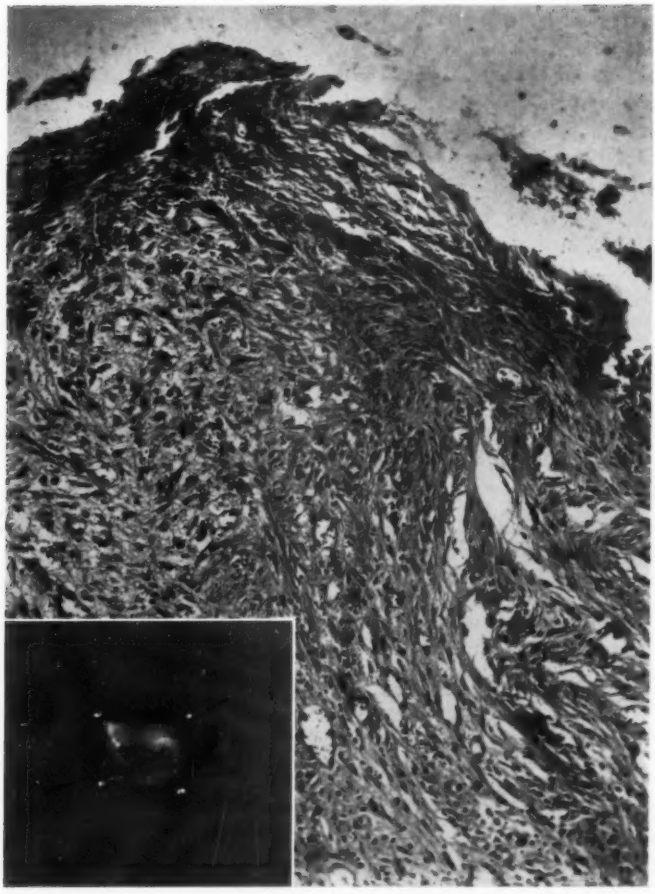

Fig. 1 (Case 1).—Small, well-differentiated fibrosarcoma of vocal cord, removed by laryngofissure. The lesion is well-localized and sharply marginated. Photomicrograph (142X) showing the rather cellular collagenous stroma, with spindled nuclei varying somewhat in size, shape and staining quality.

cells. The interlacing bundles of tumor cells and supporting stroma give a "whorl-like" appearance.

CASE 4. D.S., a white female 14 years of age, with hoarseness of four months' duration was referred with a diagnosis of "cellular fibrous tumor" based on direct laryngoscopic biopsy performed elsewhere. The initial direct laryngoscopic examination showed a rounded reddish mass in the ventricular region on the left, with downward extension partially effacing the contour of the vocal cord. Tissue removed for biopsy was reviewed by several pathologists and although the mesenchymal origin of the tumor appeared evident, the malignant character of the lesion was not definitely established. A partial laryngectomy, including partial removal of the left thyroid ala, was performed. The surgical specimen was not reported as showing histologic criteria of malignancy, a non-specific diagnosis of "cellular fibrous tumor" again being rendered.

However, regrowth of neoplastic tissue along the left aryepiglottic fold was noted after about eight months, and the lesion was now recognized as showing the histologic criteria of a fibrosarcoma of a rather cellular type. A laryngectomy was performed. The gross and microscopic character of the lesion is shown in Figure 3.

Two years and four months following laryngectomy roentgen examination of the chest showed hematogenous pulmonary metastasis, with pleural effusion on the left. Nitrogen mustard was given; for several months the patient was relatively free of symptoms and working, then died without evidence of recurrence or metastasis in the neck. In this case, the difficulties in arriving at a definitive histologic diagnosis initially undoubtedly compromised the chance of cure.

CASE 5 (neurogenic sarcoma). W.McG., a white male 59 years of age, was first seen in August, 1942. He had noted hoarseness four months previously, and shortly after this had consulted a laryngologist who found a reddish pedunculated lesion in the anterior commissure and removed it by direct laryngoscopy. The tissue had been reported histologically as "granulation tissue of nonspecific character with no evidence of neoplasm." Rather rapid regrowth of the lesion had been observed within two months.

Our initial laryngoscopic examination showed a rather large irregular reddish lesion occuplying the anterior portion of the glottis,

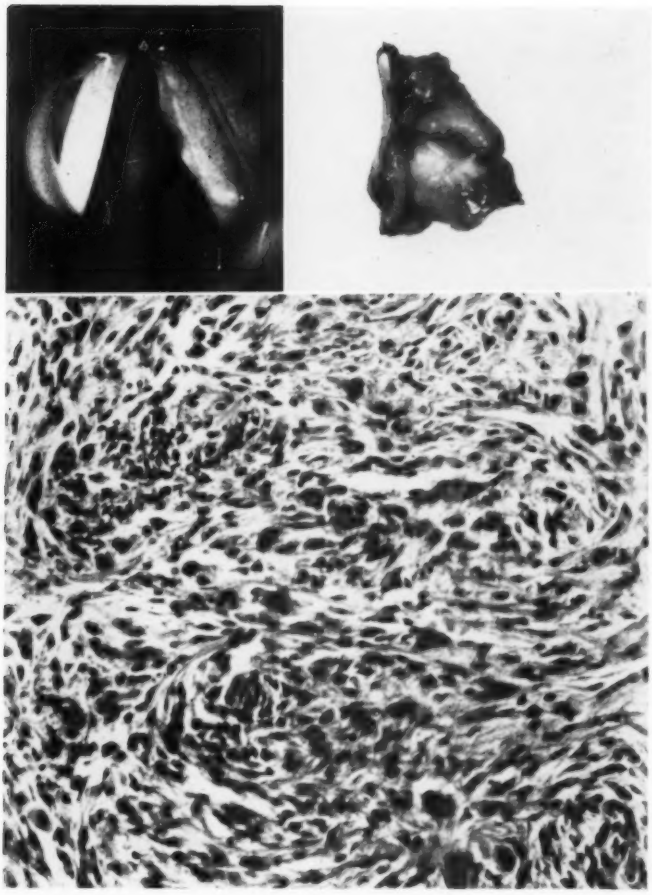

Fig. 2 (Case 3).—Fibrosarcoma of the right vocal cord treated by partial laryngectomy (fronto-lateral technique). As seen on direct laryngoscopy, the lesion is limited to the vocal cord and extends to, but not across the anterior commissure. Microscopic sections (243X) show a cellular spindled stroma. The cells have a whorl-like, fasciculated pattern. Hyperchromatism and pleomorphism are noted.

with a somewhat pedunculated attachment to the anterior extremity of the left vocal cord. The biopsy was reported neurogenic sarcoma of low-grade, and a partial laryngectomy was performed. Within three months, recurrence in the form of multiple small submucosal nodules at and above the glottic level was found and confirmed by biopsy. A laryngectomy was performed; all of the grossly evident recurrence appeared to be encompassed by an adequate margin or normal tissue.

Recurrence just within the tracheal stoma was found within two months; the upper trachea and adjacent tissues were excised and radon seeds implanted. Death from recurrence and metastasis occurred within less than one year. The microscopic appearance of the lesion is shown in Figure 4.

Most pathologists agree that differentiation between fibrosarcoma and the so-called neurogenic sarcoma is difficult. The tendency for fasciculation and palisading favor the latter diagnosis. Whether these tumors arise from the Schwann cell or from the mesodermal fibroblasts of the endoneurium or perineurium is debatable. Stout[12] firmly believes that tumors having the characteristics of fibrosarcoma, regardless of their relationship to nerve, should be called by that name rather than by the debatable term "neurogenic sarcoma." It might be added that smooth muscle tumors likewise display palisaded nuclei. Ewing[4] has described extension of neurogenic sarcoma along the epineurium, and the multiple nodular recurrences observed in this case may be indicative of such a mode of extension. It goes without saying that if the inherent character of this tumor had been fully appreciated before the initial operation, surgery of a more radical character would have been carried out.

CASE 6 (Hodgkin's sarcoma). E.C., a white female 66 years of age, was first seen eleven months following the onset of hoarseness. Laryngoscopy showed a large reddish nodular lesion involving the right ventricular region and the adjacent portion of the epiglottis, with extension to the anterior portion of the right vocal cord. The tissue removed for biopsy appeared to have the character of a lymphoma of malignant type. Further definitive classification was not accomplished at first, but slides of a lymph node removed fourteen months previously at the time of laparotomy and cholecystectomy elsewhere were reviewed and the diagnosis made elsewhere of malig-

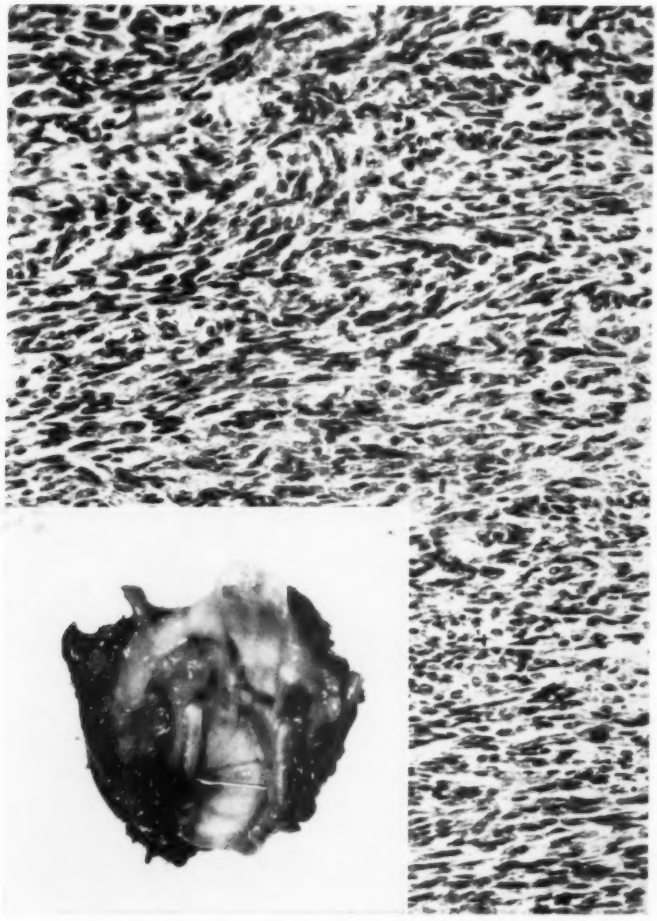

Fig. 3 (Case 4).—A more anaplastic fibrosarcoma treated by laryngectomy following recurrence after partial laryngectomy (see text). The lesion involves the entire left glottic and ventricular region and the aryepiglottic fold. The photomicrograph (243X) shows the extremely cellular character of the lesion, although the cells are fairly uniform. There is little collagen production.

nant lymphoma of the Hodgkin's type was substantiated. The laryngeal lesion has more of the histologic character of a lymphosarcoma and the exact relationship between the two lesions was not fully established; other cases of malignant lymphoma with pleomorphic manifestations have been recorded. A course of deep x-ray irradiation for the laryngeal lesion was administered.

Six and one-half years have elapsed since irradiation and no recurrence in the larynx has been observed. However, within the past year, recurrent disease were found in the pelvis and irradiation administered to this area.

CASE 7 (reticulum cell sarcoma). T.G., a white male 23 years of age, had complained of hoarseness for two and one-half months. Examination elsewhere had shown a large rather smooth mass involving the entire left vocal cord, and occluding the glottic space sufficiently to interfere with normal breathing. Several enlarged lymph nodes were palpable in the left neck. Tissue removed from the larynx and sections of lymph node were reported by the pathologist as reticulum cell sarcoma. Prompt and apparently complete regression followed a course of irradiation, and at the time of the last follow-up report about four and one-haf years following treatment, no evidence of recurrence had been noted.

CASE 8 (pseudosarcoma). J.McA., a white male 62 years of age, was referred because of hoarseness of six weeks' duration. The direct laryngoscopy showed a localized, rounded, tumor-like lesion in the anterior portion of the left vocal cord. The biopsy was reported "malignant mesenchymal tumor, probably fibrosarcoma, with carcinoma-in-situ." A partial laryngectomy by the laryngofissure technique was performed on June 17, 1959. At the time of the most recent follow-up visit, nineteen months following operation, there was no evidence of recurrence or metastasis. The microscopic sections (Fig. 5) show a cellular stroma, which is covered on one surface by a thick layer of stratified squamous epithelium. The latter in one area demonstrates severe dyskeratosis, which is interpreted as carcinoma-in-situ. The stroma is composed of interlacing bundles of spindled elements showing loose collagen production. The nuclei are frequently bizarre. Mitoses are uncommon.

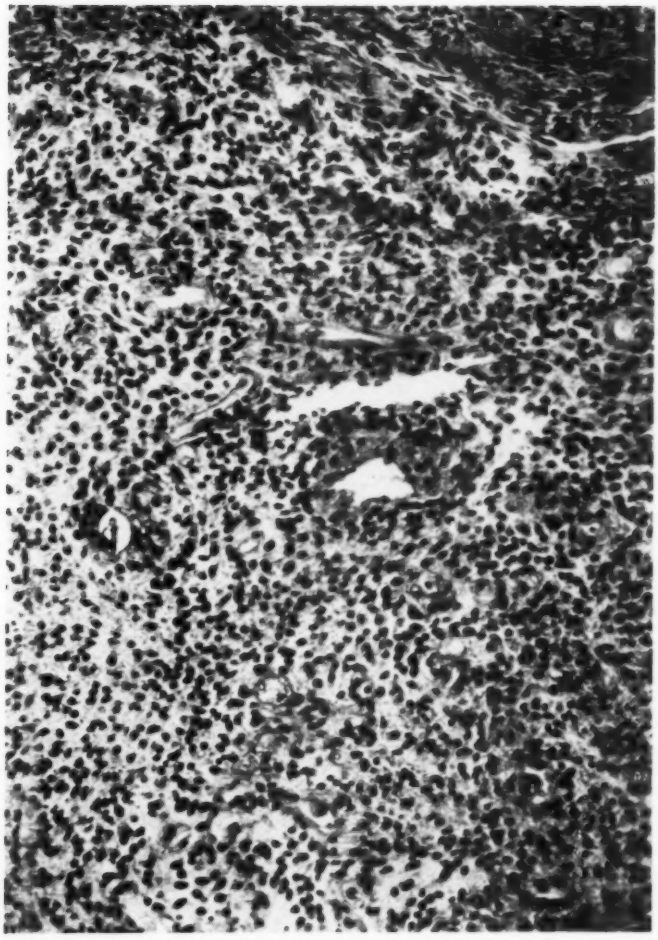

Fig. 4 (Case 5).—This lesion was felt by the pathologist to represent a neurogenic sarcoma. The photomicrograph (243X) shows a suggestion of palisading in some areas. The tumor cells are generally spindled. The stroma is loose and fibrillary.

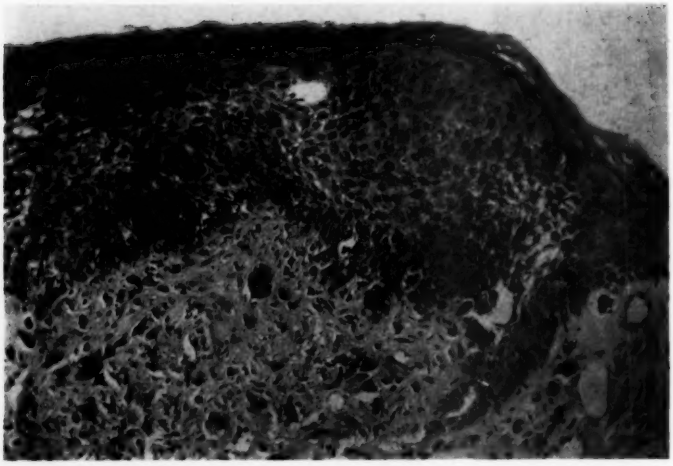

Fig. 5 (Case 8).—Pseudosarcoma. Sections of a rather well localized cordal lesion showing intra-epithelial carcinoma, with an underlying spindled stroma containing bizarre giant cells.

While this picture could represent a carcinosarcoma, we would prefer to classify it as the so-called pseudosarcoma of the type reported by Lane[9] and more recently by Baker.[2] Baker cites the opinion of Lane that the apparently sarcomatous components are not malignant locally and do not metastasize.

The terms of carcino-sarcoma, collision tumor and pseudosarcoma are somewhat confusing. Some relate the term carcino-sarcoma to the simultaneous neoplastic growth of the epithelial and stromal components of a tissue, while others attribute the carcinomatous features to metaplasia of the epithelial component. The collision tumor, on the other hand, represents an independent sarcoma and carcinoma, which in their respective growth phenomena invade one another. The pseudosarcoma is usually a pedunculated tumor, whose stroma has a sarcomatous-like pattern, but in addition there is an intra-epithelial or an invasive carcinoma. The sarcomatous element lacks the clinical behavior of a malignant tumor and does not metastasize.

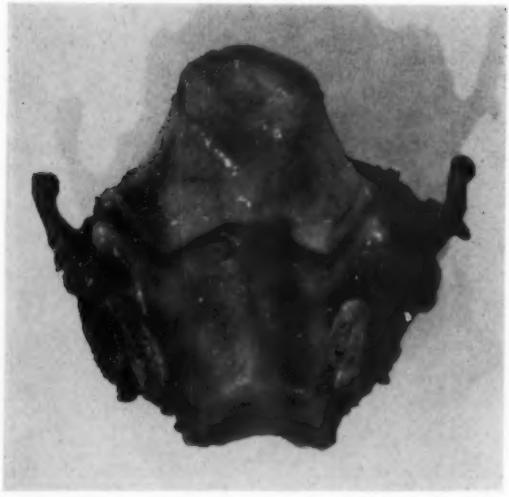

Fig. 6 (Case 9.—Pseudosarcoma, treated by laryngectomy. A previous course of irradiation had not been effective. The pedunculated polypoid character of the lesion is well shown.

CASE 9 (pseudosarcoma). E.G., a white male 69 years of age, had complained of increasing dyspnea of three years' duration, with hoarseness for about one month. He was found to have a rather marked degree of pulmonary emphysema and was orthopneic much of the time. The dyspnea did not appear to be on a basis of laryngeal obstruction, although laryngoscopy showed a grayish rather smooth and well localized lesion in the anterior commissure and on the adjacent portion of the left vocal cord. Motion of the cords was not impaired; the initial biopsy was reported as a moderately well-differentiated squamous cell carcinoma.

Because of the patient's age and advanced pulmonary emphysema with orthopnea, irradiation was given; but examination after four months showed residual neoplastic tissue in the anterior commissure and the immediate glottic region. The biopsy again showed squamous cell cercinoma, but in addition, numerous spindle-shaped anaplastic

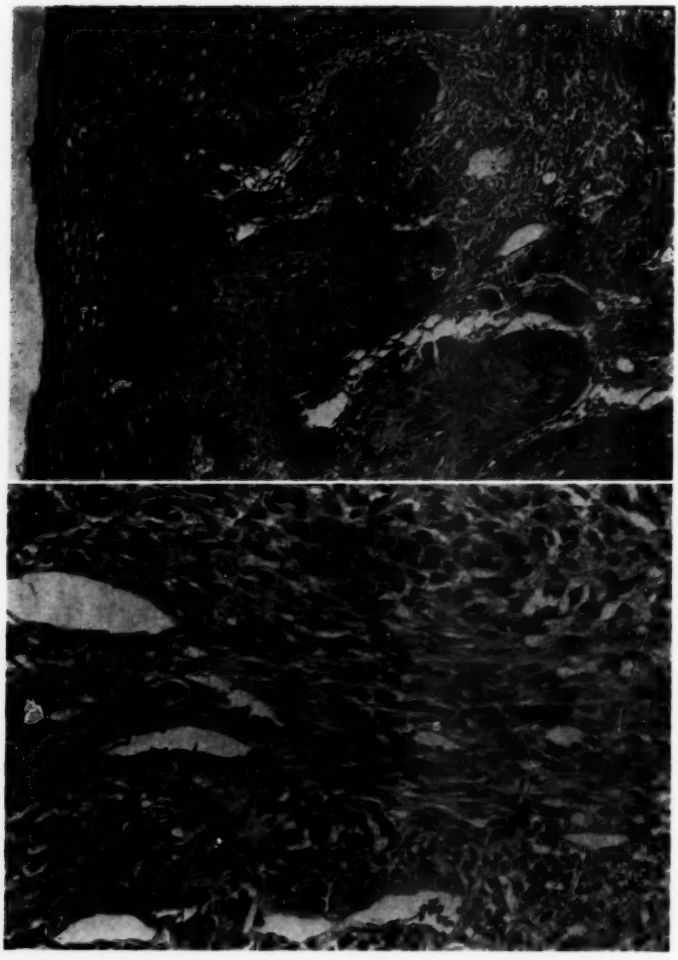

Fig. 7 (Case 9).—Pseudosarcoma. Photomicrograph at top shows early invasive squamous cell carcinoma. Below, the underlying cellular spindled stroma and the frequent mitoses.

cells in a matrix of pink intercellular material were found in some areas. A laryngectomy was performed. The character of the lesion is shown in the photograph of the surgical specimen (Fig. 6).

On a basis of the microscopic sections (Fig. 7), this case has seemed difficult to classify accurately. There is early invasive squamous cell carcinoma, the stroma has a sarcomatous appearance consisting for the most part of interlacing bundles of fibrous tissue elements, although mitotic figures are frequent and in one area there is vague suggestion of osteoid production. On the basis of these latter features we at first considered the lesion to be a carcinosarcoma, although it more likely represents a pseudosarcoma, of the type reported by Lane[9] and by Baker,[2] since their lesions have nearly always been found associated with a squamous cell carcinoma, as has also been observed by Picó.[10] This patient was last followed in March, 1961, four years and one month following operation; at that time he was living in Italy and apparently free of disease.

COMMENT

The cases presented illustrate a varied clinical behavior which, in at least two cases, did not appear predictable on a basis of the biopsy material obtained before treatment. The difficulties of accurate histologic diagnosis, as recognized by all pathologists, are exemplified by the fact that in only one of the five cases of fibro- and neuro-sarcoma was the ultimate diagnosis the same as that rendered on the initial biopsy. This is of course partially explained by the rarity of sarcoma of the larynx, but similar problems are encountered elsewhere in the body, where numerous gradations from reactive fibrosis to fibrous neoplasia are observed.

It would appear that well-differentiated sarcomas of fibrous origin may, if small, be adequately treated by conservative surgery, in our experience as well as that of Clerf[3] and Figi.[5] All three patients with lesions of this type have remained well following partial laryngectomy. The more cellular and more anaplastic lesions should undoubtedly be treated by more radical surgery initially. The problem of simultaneous neck dissection has not arisen in our cases, and will probably not occur with any frequency, as expected from the relative rarity with which sarcoma is expected to metastasize by lymph nodes. Irradiation would not be expected to be an effective form

of treatment for the fibrosarcoma, based on behavior of similar lesions in other locations, and this view has been substantiated by the experience of Johnston[7] in a recent report of three laryngeal cases.

In the case of the pseudosarcoma, as judged by the experience of Lane and Baker, the prognosis is determined by the usually associated squamous cell carcinoma. In the cases of reticulum cell and lymphosarcoma in the present group, roentgen irradiation appeared to be an adequate form of treatment.

SUMMARY

1. Clinical and pathologic features have been reviewed in four cases of fibrosarcoma of the larynx, one case of "neurogenic" sarcoma, one case of Hodgkin's sarcoma and one case of reticulum cell sarcoma. Two cases apparently representing "pseudosarcoma" are included for comparison.

2. Treatment methods and results are described. Conservative surgery appears adequate for small well-differentiated fibrosarcomas of the vocal cord. For larger lesions representing a more cellular or anaplastic fibrosarcoma, more radical operation is of course indicated.

CHEVALIER JACKSON CLINIC
TEMPLE UNIVERSITY MEDICAL CENTER

The photographic material included in this report was provided through funds of the Robert Armour Foundation of the Chevalier Jackson Clinic.

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LXVIII

A HISTOLOGICAL METHOD FOR THE STUDY OF THE SPREAD OF CARCINOMA WITHIN THE LARYNX

GABRIEL F. TUCKER, JR., M.D.

BALTIMORE, MD.
(by invitation)

Since the late 19th century a considerable number of classifications of laryngeal carcinoma have been proposed. They range from simple ones, such as intrinsic versus extrinsic[4] or vocal versus silent,[8] to classifications such as that of Barretto[1] in which the laryngeal surface is divided into many small areas. The fact that many different classifications[1,5] have been used, sometimes with conflicting definitions for a specific term, sometimes with a definition so insufficient that one cannot be certain what an author means, makes it difficult to assign categories to one's own material in a comparable fashion. Furthermore, even some of the more elaborate classifications do not take into account the submucosal anatomical structures. This situation is undergoing study by an international committee, but at present still presents a very real problem for one who wishes to classify material in a form that can then be compared with published statistics from other institutions.

The crux of this problem may be that the clinical classification of a lesion is usually based on laryngoscopic visualization and roentgenographic interpretation, whereas the pathological study of the same lesion is capable of a more precise determination of the relationship of the cancer to the structures beneath the mucosa.

From the Anatomical and Pathological Research Laboratory, Department of Otoloryngology, School of Medicine, Johns Hopkins University, Baltimore, Md. Supported in part by USPHS grant No. NINDB-B-2182 and American Cancer Society Grant No. IN-11.

PATHOLOGICAL REPORTS

To classify surgically obtained material from pathological reports presents further problems. In the first place, there is often confusion as to the precise anatomical location of the lesion within the larynx. Specific reference to landmarks is sometimes sufficiently vague that one cannot obtain a clear picture of exactly where the lesion was at the time the specimen was dissected by the pathologist. Secondly, the very nature of most pathological routines is such that the material is dissected before histologic preparation, and therefore cannot be re-examined in its original state. Thirdly, photographs of a lesion, when available, are usually of the split larynx and show only the relationship of the lesion to the laryngeal mucosa and, therefore, the deeper ramifications of the tumor are not discernible.

The key to the problem of classification probably rests with the determination of the precise anatomical relations of the lesion. The clinical relationships between the actual localization of a given lesion and many other pertinent factors are well established. Table I lists

TABLE I

Clinical appearance of lesion*	Age
Histological grade of lesion	Sex*
Classification*	Social habits
Staging*	Nature of symptoms*
Plan of treatment*	Duration of symptoms*
Prognosis*	General medical picture

a number of the facets of the problem usually recorded; those marked with an asterisk would seem to be related to actual localization of the lesion.

Upon localization depends not only the classification as to the primary site but the staging of a lesion, i.e., extension from the primary site. Clinically, the criterion for staging of extension within the larynx is usually whether or not cord mobility is lost or whether the cord is fixed in a given position. In relation to extension within

the larynx, Orton's[6] emphasis on the pre-epiglottic space, the work by Broyles[2] on the anterior commissure, and more recently Pressman's work on laryngeal compartments[7] have all pointed up the need to consider the submucosal spread of every lesion.

The above considerations demonstrate the need for a method whereby the relationship of the tumor to the laryngeal structures is preserved, thus making possible not only the study of the relationship of the lesion to normal deep structures without, in the process, dissecting the larynx, but also making possible a later review of the specimen with respect to classification of the lesion in whatever system is under study or seems pertinent at the time. To achieve these ends, it was decided the larynx should not be split or dissected but kept intact and studied by the method of serial histologic sections. According to Kernan,[9] Leroux-Robert of Paris (1936) was the first to study serial sections of laryngeal cancer; Kernan combined the use of horizontal serial sections with wax reconstruction to delineate spread above and below the glottis.

CORONAL PLANE OF SECTION

The coronal plane (or frontal plane) is best for this purpose because it is perpendicular to a majority of the laryngeal mucosa and is parallel to the respiratory axis, and because the placement along the respiratory axis is the basis of most systems of classification. In coronal sections the diseased half of the larynx may be compared with its normal mirror image in the same section.

Actual sections were projected, like lantern slides, at the meeting. The illustrations in publication are very low magnification photographs. The sections, of course, can be studied with all powers of the microscope.

PRESENTATION OF SECTIONS

Since the sections are numbered serially from the anterior to the posterior margins of the specimen, the section number gives an exact measure of the A-P depth of the specimen at which a given section was cut.

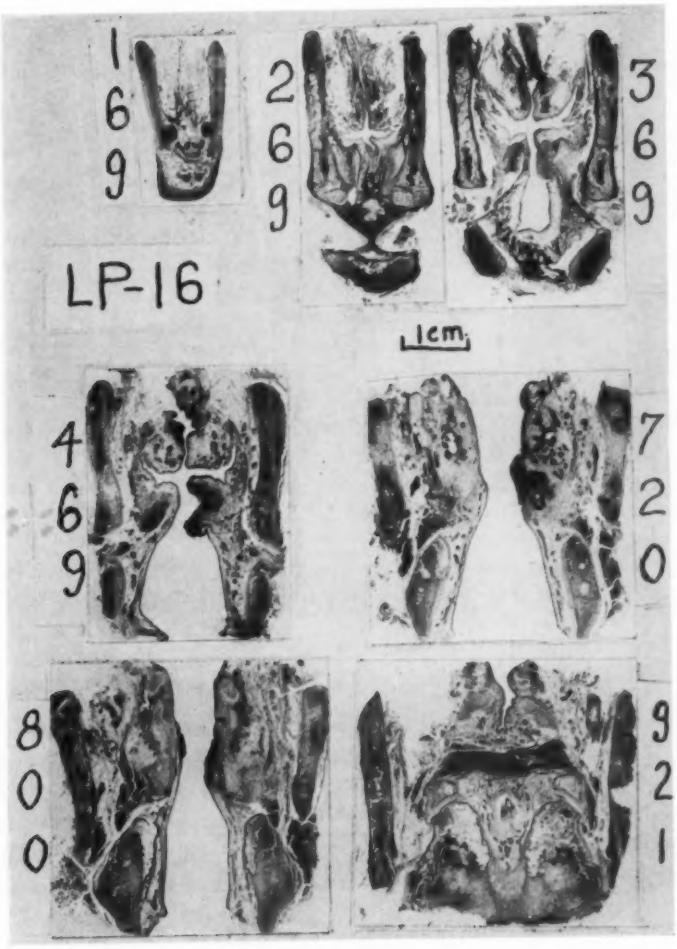

Figure 1

CASE 1. LP-16 (Fig. 1). Total number of sections, 1034.

Section No. 469—Midportion of the true vocal cords. Landmarks to be noted are the thyroid and cricoid cartilages, the true and false cords, and the ventricles extending toward the posterior limits of their respective appendices.

The lesion, squamous carcinoma, is seen to involve the undersurface of the free edge of the left true cord. It extends into the region of the vocalis muscle. Reinke's space is spared above the lesion. The irregularity of the subglottic profile stands out clearly when compared with the normal cord. Much of the space between the conus elasticus and the subglottic mucosa has been spared.

The conus elasticus stands out even more clearly in the next section shown (No. 369). This section is stained for elastic tissue and thus the conus elasticus picks up the stain. The lesion lies just below Reinke's space and just above the conus. As we move more anteriorly it may be noted that the thyroid and cricoid cartilages are approaching one another and that the mucosa is intact inside the cricoid cartilage. The saccules are better developed.

Section No. 269, similarly stained, is even further forward. The cricothyroid membrane may be seen attached to the anterior midportion of the cricoid ring.

This is the anterior limit of the lesion, just posterior to the anterior commissure.

Section No. 169, at the anterior commissure demonstrates the fusion and ossification of the inferior part of the thyroid wings. The anterior ends of the vocal ligament stand out nicely here. Above the anterior commissure the foremost part of the pre-epiglottic space is demonstrated just inside the thyroid notch.

The same lesion may be traced posteriorly:

Section No. 720, at the level of the tip of the vocal processes, shows the thyroid alae to be farther apart, the cricoid ring is enlarging, and the ventricles are no longer seen. The lesion persists just above the vocal process of the left arytenoid.

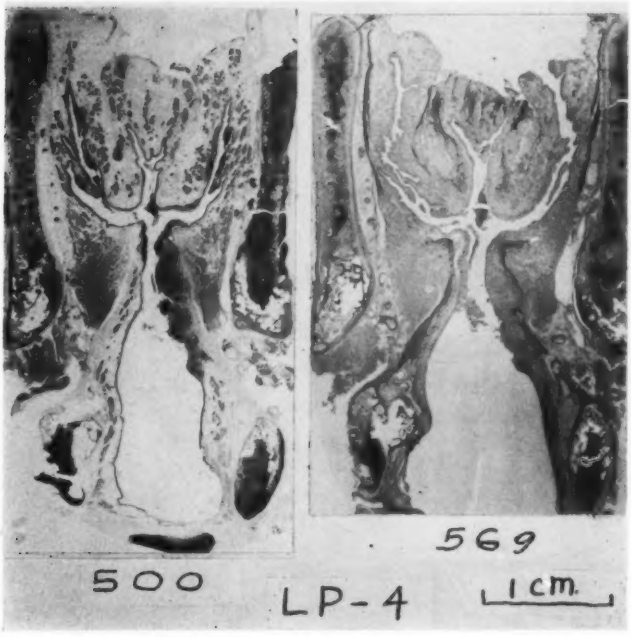

Figure 2

Section 800 shows the arytenoid cartilages better developed and the cut ends of the cricoid about to come together posteriorly. The last remnant of the lesion is on the medial face of the left arytenoid.

The last section shown from this case (No. 921) is at a plane posterior to the lesion. Here is demonstrated the lamina of the cricoid, the interarytenoideus muscle, the crico-thyroid joints, and the crico-arytenoid joints.

CASE 2. LP-4 (Fig. 2). (1300 sections). Two sections Nos. 500 and 569 are both near the midportion of the true cord; No. 500, routine H & E stain; No. 569, Orcein stain for elastic tissue. Landmarks seen here: thyroid and cricoid cartilages, true and false cords, ventricles.

Especially to be noted is the elaborate development of the laryngeal appendices. The lesion, squamous carcinoma, spreads along the subglottic surface of the left true cord. The special elastic stain shows that the conus elasticus is still intact, as is the areolar area inside the cricoid termed "the cricoid area" by Pressman.[7]

CASE 3. LP-17 (Fig. 3) (1290 sections). Section No. 572, (mid-cord), stained with Verhoeff-Van Giessen—for elastic tissue shows a much more extensive tumor. The supraglottic laryngeal structures are replaced by a squamous carcinoma which seems to stop at the level of the left ventricle. On the right side the cancer extends downward lateral to the true cord and is marginated by the right conus elasticus.

This lesion when traced forward past the anterior commissure, section No. 369, to sections No. 269 and 169 is seen to fill the pre-epiglottic space.

Section No. 960 shows the posterior extension of the lesion lateral to the right arytenoid; here it encroaches on the anterior wall of the right pyriform sinus. Also, to be noted in this section is the entrance of the vessels through foramina in the alae of the thyroid cartilage.

CASE 4. (Fig. 4) LP-9 (900 sections) is of particular interest since the carcinoma shown here occupies the region normally occupied by the laryngeal appendix,[3] or saccule.

Section No. 450 shows the endolaryngeal mucosa of the true and false cords to be intact. It was only on the third biopsy deep in the left ventricle, because of persistent fullness of the left false cord, that a diagnosis of carcinoma was made. The biopsy site is seen in section No. 410.

Sections No. 290, 250, and 210 show the anterior distribution of the lesion in planes through the anterior commissure and forward in the pre-epiglottic space just inside the thyroid notch.

PREPARATION OF THE LARYNGEAL SECTIONS

The method is essentially a modification of the technique for preparing temporal bones as used by Guild and Crowe in the otological

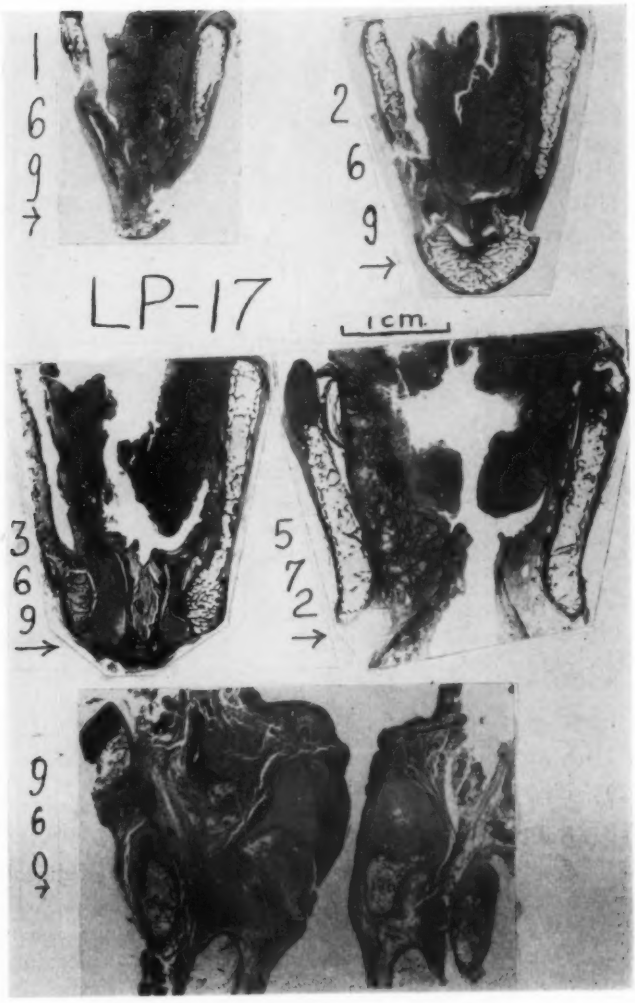

Figure 3

laboratory of the Johns Hopkins University School of Medicine for many years. This was first modified for laryngeal use in our laboratory by Broyles[2] in his classical work on the anterior commissure tendon and anterior commissure tumors.

Preservation. Material obtained from the operating room, in the case of simple laryngectomy, or from the pathological laboratory, after removal of the neck dissection part of the specimen in the case of composite laryngectomy, is placed in a large volume of 20% formalin for forty-eight hours. It is then carried through three daily changes of 10% formalin.

Decalcification. This is done with 1% nitric acid in 10% formalin. This solution is changed daily until the calcium precipitation test is negative, then carried through a 5% aqueous solution of sodium sulphate (two daily changes) and thoroughly washed in running water before dehydration.

Dehydration. This is accomplished by consecutive daily changes of alcohol of the following percentage concentrations: 35, 50, 80 (two days), 90, 95 (two days), absolute (two days) into equal parts absolute alcohol and ether, preparatory to imbedding in nitro cellulose.

Infiltration and Imbedding. This lengthy but important part of the technique is done by using increasing strengths of nitro-cellulose dissolved in ether alcohol.

6% nitro-cellulose . . . approximately seven weeks

12% nitro-cellulose . . . two weeks

20% nitro-cellulose . . . two weeks

30% nitro-cellulose . . . five weeks

35% nitro-cellulose . . . with very slow evaporation of the solvent

until sufficient hardening has occurred; this may require as long as 14 to 18 weeks. The specimen is then flooded with chloroform to complete the hardening and finally transferred to 80% alcohol. Blocks may be kept indefinitely in 80% alcohol.

Sectioning. Blocks are cut using a Spencer No. 860 microtome specially modified for large specimens. Spencer No. 865 microtome,

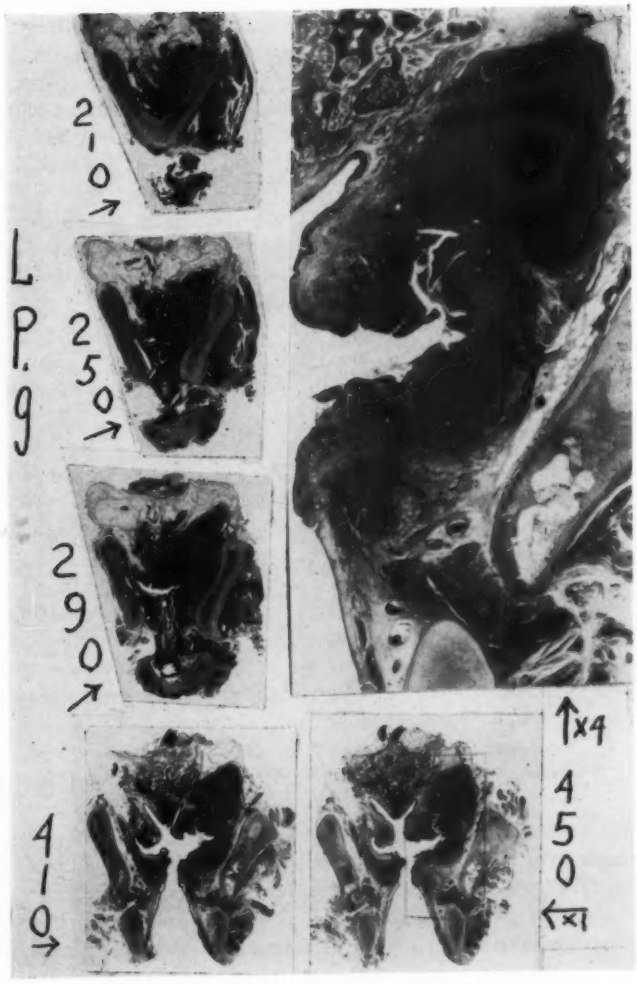

Figure 4

if available, is even more useful. The block of celloidin containing the specimen is trimmed and mounted in such a way that the posterior surface of the cricoid is parallel to the surface of the mounting block, thus placing the body of the hyoid bone and the thyroid notch uppermost. Serial sections are cut at a thickness of 24 microns. All sections are saved, and kept in serial order on numbered pieces of paper, in 80% alcohol. The average larynx, when cut in this fashion, yields 1100 to 1700 sections, depending on the exact size of the specimen.

Staining. For the first study of each specimen, each tenth section is stained, alternating between hematoxylin and eosin and Verhoeff elastic and eosin. This leaves nine-tenths of the sections available for special stains or further studies as desired.

The staining techniques used thus far have been: hematoxylin and eosin, Verhoeff elastic and eosin, Verhoeff elastic and van Giessen, Masson, PAS and Verhoeff-PAS.

Mounting. With large specimens all stained sections are mounted on lantern slide cover glass (3¼ x 4 inches) using specially cut large cover slips. With smaller specimens, the sections are mounted on the 2 x 3 glass slides used for temporal bone sections.

Storage. Due to the large size of the sections and cover slips, the mounted sections must be stored flat for many weeks before any attempt is made to store them on edge. Premature placement of the slides on edge will result in slippage of the cover slip in relation to the section and slide.

SUMMARY

By embedding the intact larynx in nitro-cellulose and serially sectioning it in the coronal plane, the relationship of the tumor to the normal laryngeal structures is preserved, and may be studied microscopically. By review of the sections obtained, one may classify the lesion by whatever criteria seem pertinent. By studying the relationship of the primary tumor to the underlying connective tissue structures, especially the conus elasticus and the laryngeal compartments, inferences may be drawn as the initial mode of spread of a given lesion. The lesion is thus placed in perspective not only with relation to the mucosal surface of the larynx, but also to the underlying anatomical

structures. It is hoped that this method will shed some light on the method of extension of carcinoma within the larynx.

I am indebted to Dr. Stacy Guild not only for his basic method of preparation of material but for his interest and advice. The senior technician, Mr. James Clarke, who spent many years with Dr. Guild, did all the technical work on the early specimens. With the financial support of the American Cancer Society, Mr. Rhine Luha has continued Mr. Clarke's work.

Words cannot express the debt which I owe to Dr. Broyles for his initial work in the preparation of sections of the whole larynx; also the debt all of us at the Hopkins owe to Dr. Broyles who, as head of the Bronchoscopic Clinic, for many years, has kept an active interest in laryngology going in our institution.

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Abstracts of Current Articles

THROAT

Histopathological Studies on the Subepithelial Basement Membrane of the Palatine Tonsils

Yamaguchi, Y.: J. of Oto-rhino-laryng. Soc. of Japan 63:122 (Jan.) 1960.

One hundred and twenty-nine palatine tonsils obtained by surgery and autopsy were examined histopathologically and histochemically. The observation was done especially on the free surface and subepithelial basement membrane of the lacuna which were comprised of argyrophil fibers and ground substances.

In the subepithelial basement membrane there was a remarkable physiological loosening, which corresponded with the inflammatory changes of the free surface. This was closely related to reticulation in the epithelial layer, the state of the follicles and the amount of fibers in the parenchyma. The loosening in the basement membrane was remarkable in infants and children.

In inflammation, the basement membrane showed marked changes ranging from "hatch" formation to partial disappearance. In many cases, these changes were seen in areas which were not directly subjected to inflammatory reaction.

The physiological loosening in the basement membrane was assumed to have been secondarily produced by the passage of lymphocytes, lymph and tissue fluid. These changes would facilitate protective action on one hand, and contact of lacunar antigen and tonsil parenchyma on the other which would contribute to the formation of antibodies.

HARA and OGURA

LARYNX

Vocal Cord Paralysis. A Roentgen Diagnostic Study

Roswit, Unger S., and *Stein, B.*: J. Radiology 75:5:741-747 (Nov.) 1960.

The tomographic aspects of vocal cord paralysis secondary to involvement of the recurrent laryngeal nerve by extralaryngeal lesions

are described and illustrated. Roentgen findngs are correlated with pathologic physiology. Patients with carcinoma of the larynx are excluded.

Because the recurrent laryngeal nerve supplies the intrinsic muscles of the larynx except the cricothyroid, the degree of involvement of this nerve governs the nature of the roentgenologic pathology. The anatomy, function and tomographic appearance of the normal laryngeal structures are reviewed. The value of this method in demonstrating improvement of paralysis as an aid in prognosis is emphasized. Eleven tomograms illustrate essential findings. 25 references are included.

JORSTAD

Serious Complications from Irradiation in Cancer of the Larynx (Accidentes graves Secundarios a la Irradiación del Cancer de la Laringe. Radionecrosis)

Guell, J.: Acta O.R.L. Ibero-Americana 11:6:489-536, 1960.

The author classifies the more serious complications of irradiation in cancer of the larynx into four main groups:

1. Fatal asphyxia developing during the course of treatment.

2. Severe asphyxia during the course of radiotherapy or subsequent to it, which requires tracheotomy.

3. Early and delayed dermatitis and perichondritis.

4. Early and delayed radionecrosis.

A summary of each of 35 clinical histories is presented. The author discusses the various factors which influence the reaction of normal and malignant tissue to irradiation, as well as the various techniques of radiotherapy. He points out the need for careful evaluation of patients in whom irradiation is to be done, both as to the local lesion and general physical condition. Careful attention to the calibration of dosage and technique of administration is essential to reduce serious seguelae to a minimum.

ALFARO

A Contribution to Laryngoscopy (Nuestra Contribucion a la Laringoscopia)

Pinart, A.: Acta O.R.L. Ibero-Americana 11:4:349-, 1960.

The subglottic area and the inferior two-thirds of the epiglottis are difficult to visualize in most cases by means of mirror laryngos-

copy. The author has devised a method of exposure of the inferior two-thirds of the epiglottis by using two mirrors. After adequate anesthesia of the pharynx and larynx with 1% Pontocaine, the patient is instructed to hold the tongue firmly. Holding the regular laryngeal mirror in one hand, the examiner introduces a second smaller mirror to the posterior commissure with the other hand. The view of the epiglottis is reflected up from the lower mirror and is easily seen in the larger mirror. The second mirror is held by a large (20 cm) malleable handle. Dexterity in the maneuver is gained quickly for routine examination of the larynx.

MOLINA

Exfoliative Cytology of the Larynx During the Female Genital Cycle (La Citologia Exfoliativa de la Laringe en el Ciclo Genital Femenin)

Perelló, J., and *Comas, J.*: Acta O.R.L. Ibero-Americana 11:4:301-306, 1960.

The cyclic variations of the exfoliating cells of the vagina demonstrated by Papanicolau and Traut have been demonstrated also in the urethra by Biot and Beltrán and in the mouth by Salvatierra and Romero. The authors investigated the possibility that this could also occur in the stratified epithelium of the vocal cords.

To carry out this investigation they examined a number of patients between the ages of 32 and 39 years, using the following technique. Twice a week the vocal cords were swabbed with a cotton applicator soaked in saline, without using anesthesia, and a smear of this material on a slide was fixed with alcohol and ether. The slide was stained by the method of Shorr which gives a pink color to the eosinophiles and green to the basophiles.

The eosinophiles were counted as well as cells which presented a cariopicnotic nucleus.

The study reveals the existence of cyclic variations in the laryngeal mucosa of the female comparable to that of the vaginal mucosa.

MOLINA

The Long-Term Follow-Up Care of Laryngectomized Patients

Reed, G. F.: J. Am. Med. A. 175:980-985 (Mar. 18) 1961.

The author makes specific recommendations for after-care for physicians not specifically trained in handling the laryngectomee.

He cautions physicians and relatives not to be over-solicitous, and suggests the patient's employer be contacted when necessary. He emphasizes that the tracheostoma must be wiped clean and dry frequently, and small crusts removed by the patient. The patient should wear some normal outer clothing over the bib, to minimize attracting attention.

Stenosis of the stoma may be treated by a plastic repair, but it is preferable to increase the size gradually by using small tubes, dilating until a No. 10 laryngectomy tube may be worn. Inspissated mucus must be treated by external humidification from wetting the bib, plants, steam vaporizers, etc., and on occasion by instilling a few drops of saline or 5% papain in the stoma. Rhinorrhea, and the loss of taste and smell, although annoying at first, correct themselves.

The esophageal voice is preferable, and must be taught and encouraged. In some, it becomes obvious that an artificial aid is necessary and the air-powered reed Bell instrument, the electro-larynx, and the electronic noise-producer are available.

The detection of recurrence and metastasis is the physician's greatest responsibility, and monthly visits are urged in the first year, and less frequent thereafter. 75% of metastases appear in the first year, and nodes palpable in a laryngectomized patient's neck, are positive in 83% of cases. The usual site of metastasis is the upper cervical chain. Recurrences are usually in the base of the tongue, suture line in hypopharynx, or tracheal stoma.

TRIBLE

The Valsalva Maneuver and the Vertebral Vein System

Batson, Oscar V., M.D., Sc.D.: Angiology 11:443 (Oct.) 1960.

Among other things, not germane to otology, the author makes the observation that when the physiology books describe the Valsalva maneuver as an "attempted forced expiration against a closed glottis" this is less than a complete statement, for the cricopharyngeus muscle also contracts, closing the pharyngoesophageal orifice. He adds that the other body cavity sphinctors, already closed, close even more tightly during the maneuver. In brief, "the larynx is the valve of the chest, the cricopharyngeus muscle the upper valve of the abdomen."

P.

MISCELLANEOUS

Fundamental Study on the Application of Radioactive Isotope for Diagnosis of Empyema Highmorii

Ichkawa, M.: J. of Oto-rhino-laryng. Soc. of Japan 63:133 (Jan.) 1960.

The author investigated the application of radioactive Na^{24} as a means of diagnosing sinus disorders. He observed the excretory and absorptive function of the mucous membrane of the maxillary sinus using the substance orally and locally.

The results were as follows:

1. The radiation counts of the secretion from the ostium of the maxillary sinus after the oral administration measured the excretory ability of mucous membrane of the maxillary sinus.

2. Decrease of the counts suggested a tendency of the mucous membrane to become fibrotic after a catarrhal and purulent stage.

3. Decrease of the counts suggested a change in the glands of the mucous membrane from a hypertrophic and dilated type to an atrophic type.

4. The delay of absorption of $Na^{24}Cl$ through the membrane suggested a change of pathology in the mucous membrane from an infiltrative type to a productive or fibrotic type.

HARA AND OGURA

Two Cases of Acute Hemolytic Anemia Following Tonsillectomy

Somerfeld, W. Z.: Dapim Refuiim, Medical Journal Kupath Holim 19:4:1-4 (Oct.) 1960.

The author describes two cases of acute hemolytic anemia which appeared following tonsillectomy:

The first case is one of an 18 year old woman who was born in Iraq and who came in for tonsillectomy because of repeated bouts of acute tonsillitis. Bleeding and clotting time prior to surgery were normal. The operation was done under local anesthesia and was uneventful. Within the following four days the patient received four injections of optalgin (4 cc each) which contains antipyrin, and twice sevenal (a barbiturate). On the fifth postoperative day the patient vomited several times and developed jaundice and fever. Her hemo-

globin was 4 gm with 1,380,000 red blood cells. Bilirubin was 3.9 mg% (indirect 3.2). The patient was treated with cortisone and blood transfusions after being diagnosed as suffering from hemolytic anemia. Ten days later the hemoglobin was 9.5 gm and subsequently her follow-up showed normal hemoglobin values.

The second case is that of a 13 year old girl who had a tonsillectomy under local anesthesia because of repeated bouts of acute tonsillitis. The patient received two injections of optalgin and felt quite well. On the second day after the operation the patient began to bleed diffusely from both tonsillar fossae which showed a massive inflammatory infiltration. The bleeding was checked with difficulty; the patient was given penicillin and streptomycin to control infection. On the sixth postoperative day a febrile hemolytic anemia appeared (6 gm hemoglobin, 193,000 R.B.C. 2.2 mg% Bilirubin). She was transfused and recovered.

The author has little doubt that these patients belong to the group described by Shiba and Sheinberg (these authors showed that immigrants to Israel from Iraq hemolised easily and showed R.B.C. glutation instability).

It is supposed that antipyrine was the cause in the first case and antipyrine or procain in the second case, though the literature does not consider antipyrine to be a hemolytic agent. Of interest is the post hoc observation that several patients of eastern origin complained of malaise and vomiting after tonsillectomy and may have suffered from unrecognized hemolytic anemia.

SADÉ

Alphachymotrypsin in Otolaryngology (L'alpha-chymo-trypsine en oto-rhino-laryngologie)

Bouche, J., Chaix, G., and *Hannequin, M.*: Les Annals d'Oto-Laryngology 77: 763-69 (Oct.-Nov.) 1960.

The authors present a clinical study with the alphachymotrypsin. The cases are divided into three main groups:

a) In otology: conductive hearing loss due to serous otitis, Tympanoplasties, adhesive otitis, deafness due to tympanosclerosis.

b) In surgery of the face and neck.

c) In radiation therapy, in cases of carcinoma.

In group *a* the enzyme is used locally as follows:

In cases of serous otitis following aspiration of the exudate, 1 mg of enzyme is injected into the middle ear. In tympanoplasties, 5 mg of enzyme (dissolved in a ten cc solution) is used to bathe the operative cavity and the middle ear. The enzyme cleans the debris of the exudate and does not affect the membranes of the oval and round windows. Intramuscular injection of the enzyme is used in groups *b* and *c*.

Good results are obtained in obstruction of the eustachian tubes and serous otitis; also in cases of adhesive otitis without ankylosis of the ossicular chain. In tympanoplasties, the enzyme enhances debridment of the ossicular chain and the windows. In surgery of the face and neck, it diminishes edema considerably; postradiation edema is also reduced.

The results are poor when ankylosis of the ossicular chain is present.

GOZUM

Injuries of the Frontoethmoidal Region (Les blessures de la region frontoethmoidale)

Andreevsky, A., and *Yovanovitch, M.*: Les Annales d'Oto-Laryngology 77:925-31 (Dec.) 1960.

Injuries of this region are produced mostly by traumas of anterior-posterior direction; traumas of lateral direction are rare. Attention should be directed especially to lesions without major tissue damage; these unapparent lesions may produce late complications. Unrecognized cases with fracture of the posterior wall of the frontal sinus may develop a cerebral abscess following a cold. The authors mention several cases diagnosed as psychosis, in which they discovered brain abscesses.

The common clinical signs of injuries in this region are ecchymosis, edema, subcutaneous emphysema and cerebrospinal rhinorrhea. Roentgen examination is very important for the diagnosis; although, negative x-ray findings do not rule out the possibility of a fractured internal wall of the frontal bone. The authors also observed herniation of the brain into the frontal sinus in cases without positive x-ray findings of fractures of the posterior wall.

They present nine case histories and suggest early exploration of the suspected cases. If the posterior wall of the frontal sinus is fractured, the condition of the dura is lacerated, plastic repair is done; if the posterior wall of the sinus is not fractured, then adequate drainage of the sinus is established.

GOZUM

Books Received

Inhaled Particles and Vapours

An international symposium recently held in Oxford by the British Occupational Hygiene Society, edited by C. N. Davies. Cloth, large 8vo., 495 pp. copiously illustrated. London, Pergamon Press, Ltd., 1961 (New York, Pergamon Press, Inc.) Price $15.00.

The book contains thirty-eight papers and the discussions which followed them. It is a comprehensive resumé of a timely subject treated from anatomical, physiological and engineering standpoints, from fundamentals to specialized phases such as asbestosis and radioactive aerosols. There is much new material in these reports. Two of the papers are in French, three in German; all the rest are in English.

The public health aspects are studied more from the standpoint of the nature of the offending substances than of the resulting diseases, and clinical thought is rather notably absent from the discussions. In a lengthy symposium such as this its omission is understandable. Since the ultimate focus of all this research is the patient, perhaps "a later conference" of which the preface contains a hint, could with profit be slanted, however slightly, toward the clinician.

Highly recommended as a basic reference work to anyone concerned with the ills of the respiratory tract.

American Medical Directory

21st edition, cloth 4to, xxxii + 1693 pp., Chicago, American Medical Association, 1961. (Price in U.S. and possessions and Canada, $45.00, all other countries, $48.00)

Whenever this tome is consulted we keep telling ourselves that the incredibly awkard format, assertedly "due to machine data processing requirements," must be the price of being able to turn out the book at all; which, however, does not save it from being easily the most aggravating reference book on our shelf.

All data of secondary importance and unalphabetizable, are neatly columnated while the critical surnames straggle in a feathery zig-zag down the middle of the column. Running a finger down the line in a quick search is impossible because there is no line.

Nor is there much relief in the arrangement of the more tractable material such as the sections on medical schools and special societies, which do not fall under the blight of automation. Undistinguished in any of the familiar ways from one another—color, typography, location—they must be sought out from among other matters by means of folios in Roman numerals.

It is hoped that, before the next edition comes along, the electronic gadget may be channeled into more conventional habits.

Diagnostic Stomatology

By *E. Cheraskin, M.D., D.M.D.*, University of Alabama School of Dentistry, Birmingham, Alabama. Cloth, 8vo., 338 pp., illustrated. New York, McGraw-Hill Book Co., Inc., 1961. Price $12.50.

The author's approach to this subject renders his book of special interest to medical men, and to the laryngologist in particular. Emphasis is placed upon the early diagnosis of systemic diseases through oral symptoms and an extensive groundwork is laid in the physiology and pathology of blood, urine and saliva. Laboratory studies are outlined for the detection of infection, chemical intoxication, nutritional disturbances, hormonal imbalance, stress disorders and malignancy. Recommended for reading and reference.

Die Stroboskopie in der Praktischen Laryngologie (Stroboscopy in Clinical Laryngology)

By *Priv.-Doz. Dr. Elimar Schönhärl*, Laryngologist-in-Chief at the University Clinic, Erlangen. Paper, 8vo., 115 pp., 50 ills., some in color. Stuttgart, Georg Thieme Verlag, 1960. (U.S.A. and Canada, Intercontinental Medical Book Corp., N. Y. Price $6.20.) In German.

Evaluation of Drug Therapy

Proceedings of a Symposium on the Evaluation of Drug Therapy in Neurological and Sensory Diseases, held at the University of Wisconsin, May 1960. Edited by Francis M. Forster. Cloth, 8vo., 167 pp., Madison, University of Wisconsin Press, 1961. (Price $4.00)

Die Behandlung der Schädelbasisbrüche (The Management of Fractures of the Base of the Cranium)

By *Prof. Dr. H.-G. Boenninghaus*, Chief of the University Ear, Nose and Throat Clinic, Frankfort am Main. Paper, 8vo., 200 pp., 98 ills., 8 tables. Stuttgart, Georg Thieme Verlag, 1960. (U.S. and Canada, Intercontinental Med. Book Corp., N. Y. Price $9.05.)

A complete clinical manual covering fronto- and laterobasal fractures involving the nose, the accessory nasal sinuses and the ear.

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